



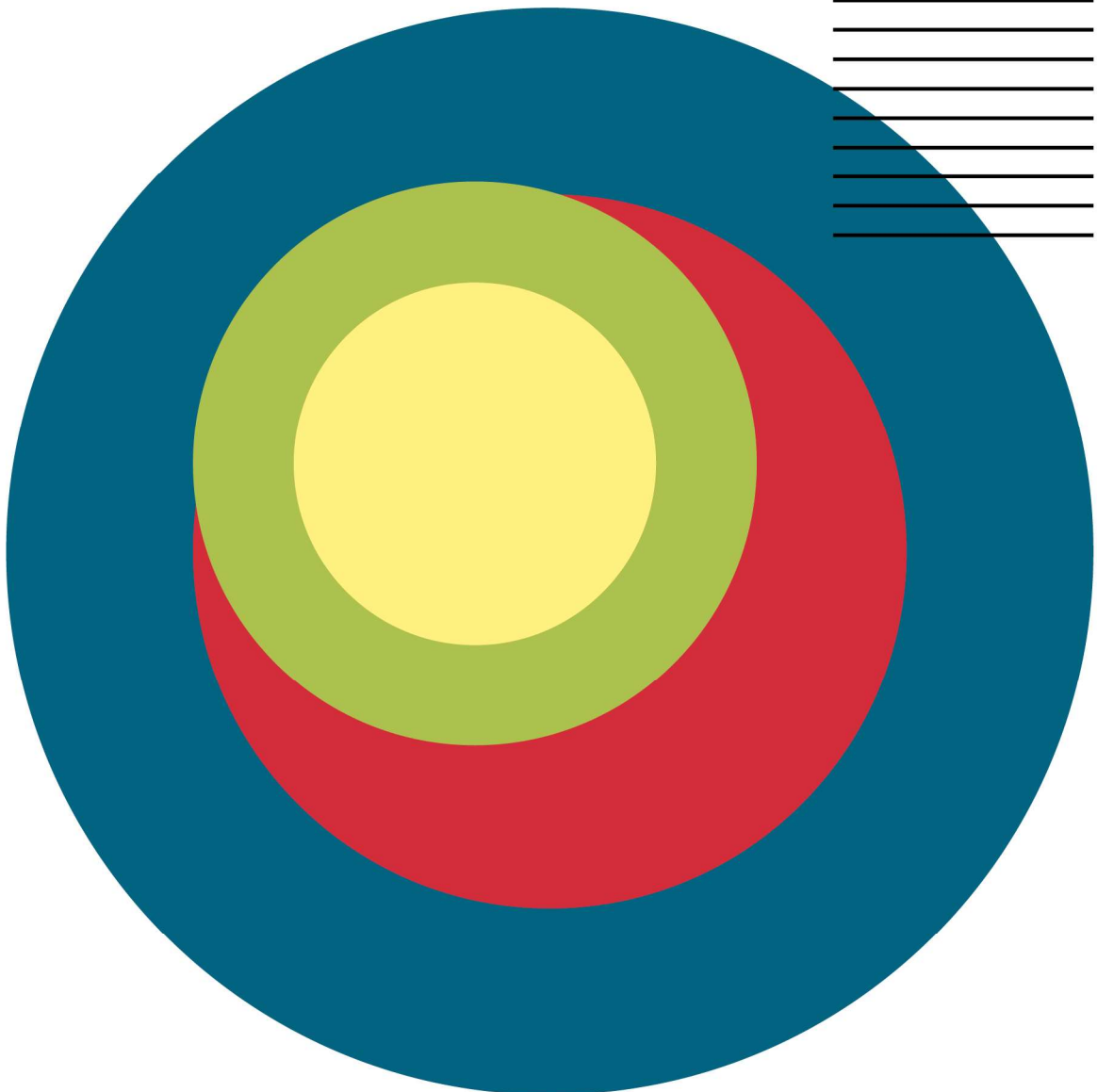
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**2018**

# Vegan diets: review of nutritional benefits and risks

Expert report of the Federal Commission for Nutrition FCN



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The Federal Commission for Nutrition  
Scientific secretariat  
Federal Food Safety and Veterinary Office FSVO  
Schwarzenburgstrasse 155  
3003 Bern  
[etr.eek@blv.admin.ch](mailto:etr.eek@blv.admin.ch)  
[www.eek.admin.ch](http://www.eek.admin.ch)

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# Contributors

## CHAIRS

- **BAUMER Beatrice**, Dipl. Food Ing. ETH, MPH, Zürcher Hochschule für Angewandte Wissenschaften, Dept. Life Sciences und Facility Management, p.o. box, 8820 Wädenswil  
beatrice.baumer@zhaw.ch
- **DARIOLI Roger**, Prof. hon UNIL, 5, ch des Fleurs, 1007 Lausanne  
Roger.Darioli@hospvd.ch

## WORKING GROUP

- **BEVILACQUA Salvatore**, Dr., CHUV, Histoire de la médecine, Bugnon 46, CH-1011 Lausanne
- **HASSELMANN Oswald**, Dr. med., Ostschweizer Kinderspital, Leitender Arzt, Kinder- und Jugendmedizin FMH, Neuropädiatrie FMH, Claudiusstrasse 6, 9000 St. Gallen
- **KEHL DUBOIS Corinne**, Haute Ecole de Santé de Genève, Filière Nutrition et Diététique, Rue des Caroubiers 25, 1227 Carouge
- **MÜLLER Pascal**, Dr. med, Ostschweizer Kinderspital, Leitender Arzt, Kinder- und Jugendmedizin FMH, Pädiatrische Gastroenterologie, Ernährung und Hepatologie FMH, Claudiusstrasse 6, 9000 St. Gallen
- **QUACK LÖTSCHER Katharina**, Dr. med., FMH Prävention und Gesundheitswesen, Klinik für Geburtshilfe, Universitätsspital Zürich, Frauenklinikstrasse 10, 8091 Zürich
- **SANTINI Diego**, Vegan Society Switzerland, 4000 Basel

## Approval

This report was approved by the Federal Commission for Nutrition on the 30 November 2017, on condition of some details to be integrated in the final published version.

# Preface

## **Prof. Dr. Philipp Schütz**

Member of the Federal Commission for Nutrition

University Medical Clinic, Aarau Cantonal Hospital and medical faculty University of Basel, Switzerland

More and more people in Switzerland are eating an exclusively plant-based vegan diet. Their reasons for doing so vary greatly, ranging from ethical and environmental considerations to the expected positive impact a vegan diet may have on health. It is therefore essential for a commission of experts with sound scientific knowledge to discuss not only the potential benefits of vegan diets, but also the risks they entail, and to make its findings available to the Swiss public in a corresponding report. With this in mind, the Federal Commission for Nutrition (FCN), a non-parliamentary advisory commission, has been tackling this important issue. The FCN has produced this report on behalf of the Federal Council and the Federal Food Safety and Veterinary Office (FSVO) and is supporting the federal government as an internal body by providing technical and scientific expertise on this topic.

The FCN's report discusses key studies investigating the connection between vegan diets and various health determinants. It is important to understand that the scientific assessments given by many observational studies are not necessarily straightforward, both from a statistical and a methodological perspective, especially since people who opt for a vegan diet often differ from those who eat a non-vegan diet in other aspects of their lifestyle too. Vegan patients, for example, tend to consume less tobacco and alcohol and generally have a more balanced diet. It is therefore difficult to establish which health effects can be attributed purely to a vegan diet and which are influenced by other factors. Taking this known limitation of many nutritional studies into account, and following an in-depth examination of the data available, the FCN's report concludes that a vegan diet can only cover all of an adult's nutritional needs if it is well planned and prepared and appropriately supplemented with vitamins and micronutrients. The positive effects of a vegan diet on health determinants cannot be proven, but there are relevant risks regarding nutritional deficiencies. Children and pregnant women are advised against adopting a vegan diet due to the risks described above. There is also a lack of sound evidence for risk groups such as patients with diabetes and pre-existing cardiovascular diseases.

Diet and nutrition are a matter of very personal choice and something each individual has the right to decide on for themselves. However, this only applies to a limited extent in the case of children and pregnant women, where the parents decide on behalf of their children. The FCN's report on vegan diets summarizes the knowledge currently available. It is intended to serve as a guide for interested readers by providing objective information on the potential benefits and risks of vegan diets, thus enabling the population living in Switzerland to make an informed decision on their own personal diet.

Philipp Schütz

Aarau, 6<sup>th</sup> March 2018

## Abbreviations

ADA	American Diabetes Association
AI	Adequate intake
ALA	Alpha-linolenic acid
BMD	Bone mineral density
BMI	Body mass index (kg/m <sup>2</sup> )
BP	Blood pressure
BW	Body weight
CAWI	Computer assisted web interview
CerVD	Cerebrovascular disease
CI	Confidence interval (95%)
CV	Cardiovascular
CVD	Cardiovascular diseases
DHA	Docosahexaenoic acid
E	Energy
EAR	Estimated average requirement
EPA	Eicosapentaenoic acid
EPIC	European Prospective Investigation into Cancer
ESPGHAN	European Society for Paediatric Gastroenterology Hepatology and Nutrition
FCDB	Food composition database
FCN	(Swiss) Federal Commission for Nutrition
FGID	Functional gastrointestinal disorder
FFQ	Food frequency questionnaire
FODMAPs	Fermentable Oligo-, Di-, Monosaccharides And Polyols
FSO	(Swiss) Federal Statistical Office
FSVO	(Swiss Federal) Food Safety and Veterinary Office
Hb	Haemoglobin
HbA1c	Glycated haemoglobin
HoloTCII	Holo-transcobalamin-II
IBS	Irritable bowel syndrome
IF	Intrinsic factor
IHD	Ischemic heart disease
IVU	International Vegetarian Union
IZiNCG	International Zinc Nutrition Consultative Group
MMA	Methylmalonic acid
MUFA	Monounsaturated fatty acids
NCD	Non-communicable diseases
OP	Organophosphates
PRAL	Potential renal acid load
PUFA	Polyunsaturated fatty acids
RCT	Randomised controlled trials
SDA	Seventh Day Adventist (studies)
SFA	Saturated fatty acids
T2DM	Type 2 diabetes mellitus
TSH	Thyrotropin
VG	Vegan (diet or individual)
VGt	Vegetarian (diet or individual)

# 1 Introduction

Current dietary recommendations, such as the Swiss food pyramid<sup>1</sup> include foods of both animal and plant origin. If a balanced omnivorous diet is followed, the daily food intake could consist in 60-70% of food of plant origin (both in quantity as in percentage of the energy intake).

Advocates of an exclusively plant-based (vegan) diet are finding more and more echoes in the popular media e.g. <sup>2,3</sup>. Along ethical and sustainability motivations, frequently health reasons are being put forward, based on anecdotal personal experience or field observations, e.g. the so-called “China Study”<sup>4</sup>.

The Swiss Federal Commission for Nutrition (FCN) concluded in its 2006 report “Gesundheitliche Vor- und Nachteile einer vegetarischen Ernährung” that a vegan diet requires a very high degree of nutritional competence in order to avoid nutrient deficiencies (e.g. vitamin B<sub>12</sub>). The FCN therefore stated that a vegan diet cannot be recommended at a general population level, particularly critical are children, pregnant women and older adults<sup>5</sup>.

Since 2006 new studies have been published, including data on the nutritional status of vegans. Furthermore some peer-reviewed recommendations state that a well-planned and supplemented vegan diet can be nutritionally adequate and healthy<sup>6,7</sup>, specific food guides have also been developed, e.g. in Spain<sup>8</sup>. The recent position of the German Nutrition Society (DGE) is however more critical and does not recommend a vegan diet for several population groups, i.e. pregnant and/or lactating women, infants, children and adolescents. In all cases supplementation and nutrition counselling are necessary<sup>9</sup>.

These recent publications question whether a revision of the 2006 FCN nutritional recommendation for the Swiss population is necessary.

## 2 Objectives of this review

Main objectives of this narrative review are first to define vegan and vegetarian diets in a historical and societal context. These aspects are taken into consideration when reassessing the conclusions of the FCN report<sup>5</sup>, focussing however on vegan diets. If possible, information should be collected on population data (percentage of population following a long-term vegan diet, typical profile of vegan followers).

Objective of this narrative review is furthermore to provide an update on current scientific evidence for nutritional advantages and disadvantages of a long-term vegan diet, including its impact on health indicators, including morbidity and mortality data on major non-communicable diseases (NCD). Other dietary patterns (ovo-lacto-vegetarians, balanced omnivorous diet etc.) are to be reported whenever these are directly compared to vegan diets, or when vegan diets are included in an overall vegetarian diet. The consequences of deficiency symptoms should be addressed; are there any specific population groups, potentially following a vegan diet, which should be screened, if yes, using which biomarkers? What supplements should be recommended (if relevant: specific recommendations for selected population groups).

These recent investigations and recommendations should be independently evaluated, with the objective to identify any aspects of the 2006 FCN report needing revision, in particular nutritional recommendations for the Swiss population. In this event, recommendations addressed to the Federal Food Safety and Veterinary Office (FSVO) and other stakeholders should be evidence-based. These recommendations will be focused on aspects pertaining to potential nutritional and health risks and benefits of a vegan diet. Reviewing environmental and ethical aspects of a vegan diet is beyond the scope of this report.



## 3 Methods

Literature search with the main keywords “vegan”, “plant-based”, “vegetarian” “diets” in bibliographic databases “Pubmed”, “Web of Knowledge”, CINAHL and “Science Direct” with languages restricted to English, German, French and Italian. Articles were retained if they published after 2006 (date of the last FCN report on this topic) until December 2017. Inclusion criteria were studies with definitions of vegan diets, studies investigating the association between vegan diets and potential health outcomes, with focus on possible nutrient deficiencies, selected biomarkers for non-communicable diseases (NCDs), and selected NCDs, in particular obesity, cardiovascular diseases, diabetes type 2 and cancer. Furthermore, the selection favoured larger primary studies (cross-sectional surveys, prospective cohorts, and randomized control studies) performed in Europe and the USA, as well as meta-analysis and systematic review articles. Studies reporting only vegetarian studies were only retained when no vegan studies were found on specific topics. References cited by the retrieved articles were searched by hand to identify further relevant articles published after 2006.

Nevertheless, this report was not conceived as a systematic review of all publications on vegan diets and health, therefore the PRISMA criteria for the search and selection of publications were not specifically applied<sup>10</sup>.

Whenever possible, the evidence degree issuing from interventional studies was also taken into account and if necessary reclassified, e.g. according to the ADA guidelines or the Cochrane model<sup>11,12</sup>.

In addition, expert opinions were collected, pertaining their clinical experience and diagnosis of possible deficiency symptoms, for critical population groups (pregnancy, infancy). Available Swiss statistical data were collected, to assess the prevalence of vegetarianism/veganism.

Frequently quoted position papers of nutrition associations and societies as well as guidelines for the prevention of NCDs were also critically assessed and discussed in the final recommendations.

Chapters were elaborated by the named authors and revised by the chair. The preliminary document was submitted to the FCN plenary for peer reviewing, and approval. Approval was given, on condition of some aspects needing more precision or details.

## 4 Historical / anthropological / philosophical aspects

**Lead author: Salvatore Bevilacqua**

### The social sciences perspective: synthesis

Veganism, as a lifestyle including and going beyond simple food choices, excludes all edible goods originating from animals. Its underlying philosophical premise is based on an ethical principle that does not accord legitimacy or necessity to any form of animal exploitation. With roots dating back to Antiquity for vegetarianism, the current vegan eating style entered progressively in a successful era thanks to the best seller “Animal Liberation” published by the Australian philosopher and bioethician Peter Singer<sup>13</sup> and the frequently mentioned “China Study”<sup>14</sup>. Veganism has its roots in the vegetarianism of the 19th century. The term “vegan” itself was coined in Scotland in 1944 by Donald Watson et al.<sup>14</sup>.

Sociological or anthropological studies on veganism are rare, although this lifestyle attracts attention from the media and possibly a growing number of people, as can be observed by the frequency of the key word “vegan” in search machines e.g. Google<sup>15</sup>, and according to the Swiss Vegan Society<sup>16</sup>. Data on the estimated prevalence of vegans in Switzerland is summarized in **table 5-2 (chapter 5)**. In Switzerland, the followers are mostly women and persons of a higher socioeconomic status than the average, according to data of the

Federal Statistical Office<sup>17</sup>. A more recent study suggests however, that more men than woman are vegan<sup>18</sup>. In this review, the French distinction between "*végétalien*" and "*végane*" will not be maintained. The first refers to an individual following a strict vegetarian diet that also excludes dairy products, eggs or honey. The second defines a person following a vegan diet but also refraining from any form of exploitation of animals, not only for food, but also for clothing and other purposes, e.g. the consumption of any product derived from or tested on animals. Veganism thus follows anti-speciesism principles of not discriminating against other animal species and respecting their different rights. According to this world view nothing justifies that animals are «naturally» available for human needs<sup>19,20</sup>.

From a socio-anthropological perspective, veganism cannot be reduced to a homogeneous set of dietary and consumption practices defining a social group *per se*. The phenomenon should be seen as a lifestyle guided by an ethical deal and a personal fulfilment search whose meanings and motivations are variable and are part of a wider system of social representations and food trends that are linked with increasingly widespread values in Western societies. These representations and values are based on a reflexive and proactive attitude mainly in regard to exploitation and animal abuse, individual health and environmental sustainability<sup>21</sup>.

### Brief historical overview

Abstention of meat consumption punctuates Western history since Antiquity. The motivations of this opposition to an omnivore society are mainly based on the rejection of the ritual sacrifice of animals; this practice was seen as bloody and immoral by some philosophers such as Pythagoras, Theophrastos, Empedocle, Porphyros<sup>22</sup>. The problem of suffering and of animal immolation as well as the belief in the metempsychosis (transmigration of the soul or reincarnation of the deceased in a living being, human or animal) divided also the first Christians<sup>23</sup>. At the end of the 18th century groups of Protestant dissidents first, followed by philanthropic movements, advocating vegetarianism appear in England. The utilitarian philosopher Jeremy Bentham asserted that the animal suffering, like the human suffering, was worthy of moral consideration, and he regarded cruelty to animals as analogous to racism<sup>13</sup>. The first vegetarian society was created in England in 1847 by members of the Bible Christian Church<sup>22</sup>, and the International Vegetarian Union was founded in 1908<sup>24</sup>. In Switzerland a vegetarian society was founded in 1880<sup>22</sup>. This spiritual and moral vegetarianism reached the United States during the 19th century where it was transformed into a hygienist movement. In the United States and in Europe, particularly in Switzerland and in Germany, an expansion of vegetarianism can be seen, particularly in health facilities applying the precepts of the „Lebensreform“.

### Socio-symbolic dimensions of a vegan lifestyle choice

The three major motivations – compassion for the animals, quest for “pure” food and asceticism<sup>22</sup> - for a meatless diet advocated in Antiquity remain relevant (the first in particular) to understand the motivations and unconscious symbolic challenges of the contemporary veganism. Thus, in the heart of the “vegan culture” we find the conception of respect for animal life, which refers to the myth of paradise where people and animals used to live together peacefully, living exclusively on the fruits of a prodigal mother-earth. In this myth, violence inflicted on animals by men to dominate and feed on would ensue from a primordial sacrifice breaking the original harmony of the world and demanding, therefore, purifying rites (ritual slaughter) whose function is to “civilize” the act of killing. For anthropologists, this ritual sacrifice assumes a control function of so called “food murder”, whose goal is to attest, by appealing to the sacred, symbolic discontinuity between humans and animals (including mammals) to legitimize and thus make edible the sacrificed being. However, the current antispecism stands on an ethical and moral vision that involves responsibility and even guilt in human domination and violent destruction of animals for consumption. The process that leads an individual to consume exclusively plant products reflects an ethical awareness and a critical choice (or even a duty) to break with properties, nutritional and symbolic, historically and culturally attributed to killed animal flesh. The meat diet is, in fact, ambivalently associated with force, with power, but also with impurity and sin. The ensuing

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<sup>a</sup> The Cathars, although piscivorous, are also an example.

"food decision" is the result of a process of rationalization and incorporation by the individual, which, depending on its cultural frame of reference and its successive socializations, leads him to "choose" one or other diet and to define himself in relation to the "opposite" one.

Various studies point out that vegetarians are not a homogeneous entity. Their biographies, their motivations, their interests, their spirituality and their therapeutic approaches, nevertheless show some recurrences. It would be appropriate to apply this pluralistic approach to veganism too.

As shown by qualitative surveys collecting the stories of people having turned to vegetarianism<sup>25,26</sup>, subjects explain their conversion - gradual or sudden – as having begun at key moments of their life cycle (adolescence, leaving home, birth of a child, separation, divorce...) or due to either serious or chronic health problems. The acute awareness of certain philosophical, ecological or political (North-South relations) themes also appears in the words of the respondents. Stories also refer to specific experiences that are often reliving memories of childhood or youth (like the "put to sleep" of a pet or a visit to a slaughterhouse). Especially older followers also describe forms of asceticism (fasting) and sexual abstinence. Even if one or the other pattern is predominant, motivations and practices often combine to result in a particular food order and a way of life (first meaning of the Greek term *diaeta*). The experience of the most convinced vegetarians tends to validate the thesis of a true "alternation", that is, according to Berger & Luckman<sup>27</sup>, a conversion or transformation of a social identity resulting from the internalization of a different meaning system. Such experience is often described through evocation of emotionally strong moments, mention of resources and support from charismatic persons, length and density of learning, and comprehensive incorporation of experiences learned during internships and courses.

Environmental concerns also lead to a general preference for organically grown food<sup>28</sup>. In a German study with over 800 vegans the major motivations for choosing a vegan diet were objections to mass animal husbandry, environmental concerns and health issues<sup>29</sup>. In a USA study with both vegetarians and vegans (n=312), ethical reasons (animal rights, ethics, spiritual beliefs, environment and non-specified other ethical reasons) were more commonly (75%) given as a reason for becoming vegetarian / vegan. Health reasons (general health, weight loss, other health-related reasons) were mentioned by 18.5% of the participants, other minor reasons were taste, family/friends, upbringing, politics and saving money<sup>30</sup>. A recent qualitative study performed in Germany also concludes that ethical and political considerations are the main motivations for a vegan lifestyle<sup>31</sup>.

## 5 Definitions and statistics

**Lead author: Beatrice Baumer**

As seen in chapter 4, vegetarian diets are plant-based diets, characterized by abstention from the consumption of foods of animal origin, the extent of which can vary, but generally excludes consumption of animal flesh. Swiss food legislation has defined conditions required for the labelling of vegetarian foods (article 40)<sup>32</sup>:

- a) "Vegetarian", or "ovo-lacto-vegetarian", whenever neither ingredients, nor processing aids, of animal origin are included, with the exception of milk, milk components, such as lactose, eggs, egg components and honey.
- b) "Ovo-vegetarian", whenever neither ingredients, nor processing aids, of animal origin are included, with the exception of eggs, egg components, or honey.
- c) "Lacto-vegetarian", whenever neither ingredients, nor processing aids, of animal origin are included, with the exception of milk, milk components and honey.
- d) "Vegan", whenever no ingredients of animal origin are included.

These definitions are consistent with a large part of the reviewed literature where, however, veganism also excludes processing aids of animal origin. The scientific literature selected for this review included other definitions for vegetarian diets, mainly defined by the food groups of animal origin still included in the diet, as summarized in **table 5-1**. This classification is not standardized, and most studies rely mainly on self-reporting

or on general questions concerning intake of food items of animal origin, based on food frequency questionnaires developed for the general, omnivorous population. In this review, focus will be on general vegan diets, extended to vegetarian diets only when the vegan data are insufficient.

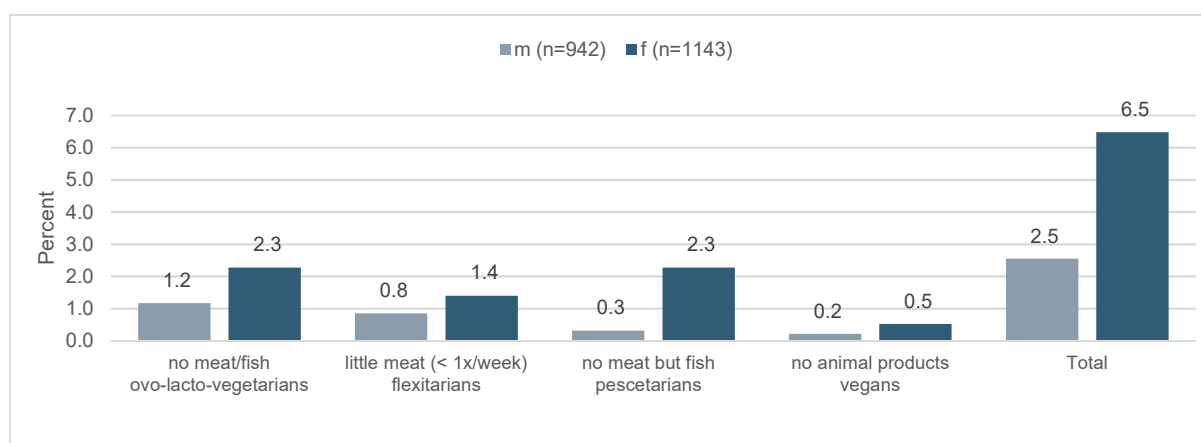
Data on the prevalence of vegetarians and vegans in Switzerland are scarce and summarized in **table 5-2** and **figure 5-1**, but suggest a range from 0.2% (menuCH data) to maximum 3% (Swissveg data) of the adult population following a vegan diet, and approximately 6% a vegetarian diet. A higher prevalence of vegan/vegetarian woman compared to men is consistent with existing data, as summarized by Ruby<sup>33</sup>.

**Table 5-1: Definitions of vegetarian and vegan diets in the scientific literature\***

Type of diet (selection, preparation)	Summary of definitions collected from numerous sources, abridged
<b>Flexitarian (semi-vegetarian) / meat reductionism / reductarian</b>	Occasional inclusion (less than once per week) of flesh foodstuff (meat, poultry and fish) and permits eating all other animal products (e.g. eggs, milk, honey).
<b>General vegetarian diets</b>	Whenever not specified, a vegetarian diet is often an ovo-lacto-vegetarian diet, as also defined in the Swiss legislation (see above).
<b>Pescetarian (pesco-vegetarian)</b>	Includes seafood/fish, but not flesh of other animals (meat, poultry), and permits eating all other animal products (e.g. eggs, milk, honey). This diet is sometimes included in the semi-vegetarian group.
<b>Pollo-vegetarian</b>	Poultry is the only animal flesh consumed, as well as dairy and egg products. This diet is sometimes included in the semi-vegetarian group.
<b>Ovo-lacto-vegetarian</b>	Excludes all types of flesh foodstuffs (meat, poultry, fish), but permits eating all other animal products (e.g. eggs, milk, honey).
<b>Lacto-vegetarian</b>	Excludes flesh foodstuffs and eggs but allows dairy products, honey.
<b>Ovo-vegetarian</b>	Excludes consumption of all animal products with the exception of eggs.
<b>Vegan, vegetarian</b>	<p>Diet which excludes all animal products (both as ingredients and processing aids, the latter being an important aspect, not mentioned in the Swiss legislation). An exception is human mother's breast milk, given voluntarily. Veganism can also imply excluding all items of animal origin (e.g. made from wool, silk, leather materials).</p> <p>In French-speaking areas a distinction is made between "<i>végane</i>" and "<i>végétalisme</i>" (see chapter 4). Other sub-categories of a vegan diet are:</p> <ul style="list-style-type: none"> <li>• <b>Vitarian (raw vegan)</b>: Permits consumption of organic, raw and fresh foods only. Excludes coffee and tea.</li> <li>• <b>Fruitarian</b>: Excludes flesh foodstuffs, animal products and vegetables, cereals → permitted are only fruit, nuts, seeds, which can be gathered without damaging the plant</li> <li>• <b>Sproutarian</b>: Eating foods in the form of sprouted plant seedlings, such as grains, vegetables, fruits.</li> </ul>

**Table 5-2: Prevalence of vegetarians and vegans in Switzerland**

Study / article	Data
<b>Proviande Switzer-land<sup>34</sup>, 2012</b>	A representative study (800 interviews) performed on behalf of shows that 6% of the participants are vegetarians
<b>Swiss Food Panel of the ETH Zürich<sup>35</sup>, 2013</b>	Approx. 3% of the participants are vegetarians
<b>Swiss health surveys, performed in 1992, 1997, 2002, 2007, 2012<sup>36</sup></b>	Participants were asked about their meat and fish consumption. The percentage of meat abstainers has increased slightly over the years (from 1.9 to 2.7% of the sample). Abstention from fish is more frequent, with percentages between 9.2 and 10.6%.
<b>menuCH 2014-15 (24h-recall GloboDiet)<sup>37</sup></b>	According to this representative study, the corrected data suggest that in average 4.7% of the adult population follow a vegetarian diet (6.5% of adult women, 2.5% of adult men). The data are not clear enough to identify vegan diet followers, but suggest a prevalence of approx. 0.38%, 0.52% (n=6) of the women and 0.21% (n=2) of men, details in figure 5-1
<b>Swissveg / Demoscope 2017<sup>18</sup></b>	The survey was performed in January/February 2017, with 1'296 participants (CAWI ad hoc), between 15 and 74 years old, and in the German and French speaking regions. The prevalence of vegans was of 3%, with a confidence interval of +/- 0.9%. These data are not comparable to the menuCH data (e.g. age groups, recruiting and focus on a representative population sample)

**Figure 5-1: menuCH-data 2014-15 (24-recall, GloboDiet, 2017, not yet published)<sup>37</sup> m= male, f= female**

Little is known about the typical duration of a vegan diet. The most recent study performed in Switzerland confirms that a majority of vegans (76%) have been following a vegan diet for less than 5 years<sup>18</sup>, Schüpbach et al. report an average duration of 3.0 years (1.0-18.0)<sup>38</sup>. In a USA cross-sectional study with 312 vegetarians and vegans it was observed that participants choosing their diet for ethical reasons had been following the diet for a longer period (mean 9.97 years) than participants who mentioned health reasons (mean 5.9 years), this study is however based on self-reported data, and a selection/response bias is possible<sup>30</sup>.

Even less is known about the prevalence of relapsed vegans. A cross-sectional survey performed in 2014 in the U.S.A. estimates a prevalence of 0.5% vegans, but of 1.1% former vegans. The data on the duration of the vegan diet are unclear, 34% of the former vegans followed this diet for less than 3 months. 37% of former vegans are however interested in re-adopting a vegan diet in future, often for health reasons. This survey suggests that some individuals will switch between omnivorous, vegetarian and vegan diets throughout their lifespan, and that even vegans cannot maintain an absolute diet purity<sup>39</sup>. This type of eating pattern could alleviate some typical potential nutrient deficiencies discussed in the following chapters, in particular for vitamin B<sub>12</sub>, and health outcomes, but no specific studies were found on the topic.

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### Amendment to the 2006 report

There are now more data on the prevalence of vegetarianism and veganism in Switzerland. The data still have to be considered as estimates, with approx. 0.2-3% of the adult population following a vegan diet. The samples size of the surveys are not large enough to have more definitive data, different sampling and methodologies hamper comparisons and the identification of trends. Further monitoring is recommended, also taking into account the duration of the diet, the motivation for this dietary choice, the frequency of dietary deviations and closely monitoring the vegan trend among teenagers.

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## 6 Vegan diets from the nutrient perspective

**Lead author: Beatrice Baumer**

Recent cross-sectional and cohort studies provide data on the diet of healthy adult vegetarian and vegans in Europe, these studies will be the main sources for assessing the potential nutrient-based risks and benefits linked with a vegan diet. In Switzerland, the dietary intake was assessed with a three-day weighed food record (analysed with the EBIS pro software) + questionnaire and measuring plasma concentrations of vitamins and minerals<sup>38</sup>. In Denmark a four-day weighed food record was performed, using a 52-item FFQ (including vegan protein sources, such as tofu, meat alternatives) and the Danish FCDB<sup>40</sup>. In the United Kingdom the EPIC-Oxford cohort study used specific questionnaires<sup>41</sup>, these results were updated in 2016<sup>42</sup>. A further UK study was performed by analysing the data of the UK Biobank, based on 24-h dietary assessments. This study focused on protein intake and on protein sources<sup>43</sup>. In Belgium dietary intake was assessed by FFQ and using a Belgian FCDB<sup>44</sup>. In Finland a three-day food record was performed, combined with plasma, serum and urine analysis<sup>45</sup>. In the French web-based NutriNet-Santé study dietary data were collected using 24-h reports and the daily nutrient intakes were calculated using a specific NutriNet FCDB, data were adjusted for sex, age and total energy intake<sup>46</sup>.

Details for these studies are given in **appendix II**, due to methodological limitations these studies were classified as being of evidence level C.

### Macronutrient intakes

Based on the dietary records rough estimates were made for the intake of **macronutrients**, as summarized in **table 6-1**. This overview suggests that a vegan diet can cover the macronutrient recommendations (carbohydrates, fats, including low SFA, dietary fibre, total energy), as reported in all studies. The standard deviations are however wide, for the Swiss sample, the mean protein intake of 65 g could corresponds to an adequate quantitative intake for healthy adults, but with a variability of +/- 21 g (**table 6-1**). Generally, these data indicate that some participants are not covering their protein needs. The published data do not however provide specifics on the participants with the lower protein intake, e.g. gender, age, body weight, PAL<sup>38</sup>. None of the studies specifically described a protein deficiency. The small number of participants and a possible selection bias (intrinsic motivation of participants to participate, "healthy volunteer effect") must however be considered<sup>38</sup>.

Even in a well-balanced omnivore diet, about 30-40% of the protein intake is provided by food of plant origin (for exemplary calculations refer to the table in appendix I). This percentage increases when protein-rich vegetable products (e.g. pulses, soybean-based products) are included: An adequate intake of these food items theoretically covers protein needs. The essential amino acid needs could also be covered, by eating a variety of protein-rich foods during the day. In the EPIC-Oxford study qualitative aspects of the protein intake were assessed with a cross-sectional analysis. Vegans (n=98) covered 2.8% of their energy intake with protein from soya products and 9.6% with protein from non-soya plant products, the intake profiles for amino acids was significantly lower than those of all other diet groups, in particular for essential amino acids (refer-

ence: omnivores). Both vegetarian and vegan diets had a lower intake of non-essential amino acids, compared to omnivores. Plasma analysis however, showed that only few amino acids (lysine, methionine and tryptophan) were significantly lower in vegans<sup>47</sup>. These studies all show that attention is needed to cover both qualitative and quantitative (amino acid) needs. Furthermore, other aspects, such as the possibly lower digestibility and skeletal muscle anabolic response to plant proteins, were not taken into account<sup>48</sup>.

These results show that for the assessment of the nutritional status more accurate data are needed, e.g. there is a suspicion of under-reporting in the UK data, the data should be stratified at least by sex (see differences in the UK and Danish data). The data do not take into consideration finer details, such as the impact of the underlying motivation for following a vegan diet, which could have an impact on the eating pattern. The most recent Swiss study shows that most vegans are motivated by ethical and environmental concerns, only 35% follow this diet for health reasons<sup>18</sup>.

As recognized by Radnitz et al. with an international online survey (n=246 participants) health-based or ethically-based vegan choices can influence the eating patterns, with the first (health motivated vegans) more frequently associated with healthier food choices (more fruit and fewer sweets), whereas ethically driven vegans reported a higher likelihood of taking supplements, soy-based products, and high-polyphenol beverages<sup>49</sup>. Dyett et al also report different lifestyle and dietary behaviours among the 100 USA study participants, depending on the underlying reason for their vegan choice<sup>50</sup>.

When comparing the Swiss vegan/vegetarian data<sup>38</sup> with the average data collected during the Swiss survey menuCH<sup>51</sup> the energy, fat and carbohydrate intakes are comparable to the general study, with however a lower protein intake and a higher dietary fibre intake. Further research is necessary in evaluating if differences in eating patterns, depending on the motivation, could impact the macronutrient intakes.

**Table 6-1: Macronutrients intake (mean / median, adjusted and rounded values) in vegan diets, in different European countries, compared to Swiss recommendations (for healthy adults) for details on the study design refer to appendix II**

	Aggregated FCN/DACH recommendations <sup>52,53</sup>	General Swiss data menuCH <sup>51</sup>	Switzerland <sup>38</sup>		Denmark <sup>40</sup>		UK <sup>42</sup>		UK <sup>43</sup>	Finland <sup>45</sup>	Belgium <sup>44</sup>	France <sup>46</sup>
<b>Participants</b>	Healthy adults	Adults n=2'085	VGT n=43	VG n=43	VG m n=33	VG f n=37	VG m n=269	VG f n=534	VG M= 105, F = 146	VG (m: n=6, f: n=16)	VG n=104	VG = 789
<b>Energy (kcal/day)</b>	1'700-2'500	2'232	2'263 (+/-559)	2'469 (+/-596)	2'797	2'065	2'132	1'879	M: 2'037 F: 1'842	2'150	2'383	(used for adjustment)
<b>Total fat (E) % E or g/d</b>	20-35 % (max 40) → 40 -100	91	93	96	86.7 (63-105)	65.1 (49-79)	72	64	Not reported	88 (+/-37)	68	72.7 (+/-19.7)
<b>SFA (%E or g/d)</b>	< 10% E → 19 - 28		34	20	17	13	16	14	Not reported	21 (+/-9)	21	19.4 (+/-11.2)
<b>Carbohydrates (% E or g/d)</b>	45 - 55% E < 191-344	234	267	324	332	222	288	253	Not reported	252	336	235.7 (+/-45.0)
<b>Added sugars*** (% E)</b>	Max 10% E < 42 -62		131	180	18**	22*	120	110	Not reported		156	105.3 (+/-33.7)
<b>Dietary fibres g/d</b>	30	21	31	52	56	40	30	28	Not reported	41	41	34.1 (+/-8.4)
<b>Proteins (g/kg BW)</b>	Min 0.8 g/kg BW	84	64 (+/-21)	65 (+/-21)	75.5 (66-96)	59.1 (51-67)	0.91 (+/-0.3)	0.99 (+/-0.34)	M. 14.8****% of E (=75.4 g) F: 16.4%**** of E (=75.5 g)	74 (+/-30)	82	62.0 (+/-22.5)

\* data (unpublished)<sup>37</sup>, stratified by eating behaviour, show that vegans & vegetarian have a similar total energy intake, but a significantly lower protein intake (11% of the energy intake), compared to 15% in the omnivore group, the vegan/vegetarian group has a higher carbohydrate and fibre intake.

\*\*only added sugars

\*\*\*"Sugars" definitions are not always included, in general it is the sum of simple carbohydrates (mono- and disaccharides)

\*\*\*\*: as quantities of major protein source foods, i.e. not protein content. Moreover, protein from cereal sources was not taken into account

VGT: vegetarian; VG: vegan; m: male; f: female; E: energy; BW: body weight; SFA: saturated fatty acids.



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### Amendment to the 2006 report

The recent European studies contribute to a knowledge gap in the previous report, with estimates for the macronutrient intakes for vegans. The specific data show that a vegan diet can cover macronutrient and energy needs. The large variation in intakes, as seen in the Swiss sample, does however confirm that a vegan diet needs good planning, in particular to cover quantitative, and possibly also qualitative, protein needs.

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#### 6.1 Positive nutrient aspects of a vegan diet

In general all diet forms providing a high intake of fruit and vegetables have a positive effect on health, as confirmed most recently by Aune et al.<sup>54</sup>. The above-mentioned studies do not however report the estimated intake of different food items, which would be of great interest, because it is generally assumed that a vegan diet is rich in fruit and vegetables. This assumption was one of the salient basis of the former FCN report. Some fruit and vegetable intake data have been published and are summarized in **table 6-2**. Vegan diets include more fruit and vegetables than other diets, the average values show that general recommendations of 2 portions of fruits (200-240 g) and 3 portions of vegetables (300-360 g) are fulfilled. These data show however, that fruit and vegetable intakes vary among the different studies, furthermore, the standard variations, when reported, indicate a wide variability in intakes in the individual studies. Based on the data it is not evident to conclude that a vegan diet is per default rich in fruits and vegetables. Therefore, not all vegans can unquestionably benefit from the advantages of a plant-based diet with a high fruit and vegetable intake (i.e. with more than 4-5 portions of vegetables and fruits per day).

A balanced vegan diet can cover macronutrient needs, as seen above. In the Belgian study food intake data were evaluated with a Healthy Eating Index and the vegan diets were shown to have the highest scoring with this index, compared to the omnivores in the study group<sup>44</sup>. A high intake of foods of plant origin (fruit, vegetables, cereals, pulses and nuts), covers the needs of many micronutrients typically found in these food groups. Compared to ovo-lacto-vegetarians and omnivores, vegans have a higher intake resp. status for several nutrients: magnesium, vitamins C, B<sub>1</sub>, B<sub>6</sub>, folic acid, as recorded and measured in the Swiss study by Schüpbach et al.<sup>38</sup>. It can be expected that a vegan diet also provides a wide array of phytochemicals (e.g. carotenoids, phenolics), with potential health benefits<sup>55</sup>.

As described by Platel et al. for example the use of spices, onions and garlic as well as acidic fruits in the diet enhances the bioavailability of trace elements (e.g. iron) from plant foods<sup>56</sup>. This may contribute to a sufficient supply with trace elements from sources with rather poor bioavailability and could counter the negative effect of phytic acid, discussed below<sup>31</sup>.

**Table 6-2 Fruit and vegetable intake in vegan diets compared to other diets** (in g / day, if not otherwise stated)

Country	Fruit consumption (g/day)		Vegetable consumption (g/day)	
	Vegan diet	Reference group	Vegan diet	Reference group
<b>Finland (Elo-rinne et al.)<sup>45</sup></b>	Fruits: 223 +/-186 Berries: 31 +/-44 Fruit juices: 103 +/-169 Berry juices: 34 +/-73	(non vegetarian) Fruits: 266 +/-185 Berries: 114 +/-164 Fruit juices: 38 +/-111 Berry juices: 4	277 +/-186	246 +/-159
<b>France (van Audenhaege et al.)<sup>57</sup></b>	297.0 +/-292	Lacto-vegetarians: 265 +/-144.9 Ovo-lacto-vegetarians: 317.6 +/-228.3 Pesco-vegetarians: 124.7 +/-73.3 General population: 173.4 +/-135	459 +/-300.2	Lacto-vegetarians: 286.1 +/-112.9 Ovo-lacto-vegetarians: 381.8 +/-144.8 Pesco-vegetarians: 339.1 +/-169.8 General population: 170.1 +/-79.9
<b>France (Allès et al.)<sup>46</sup></b>	364.2 +/-171	Vegetarians: 290.6 +/-170.4 Meat-eaters: 245.1 +/-210.8	366 +/-123	Vegetarians: 285.8 +/-121.7 Meat-eaters: 216.4 +/-150.6
<b>UK (Appleby et al.)<sup>41</sup></b>	Vegetarian and vegans: 293 +/-244	Regular meat eaters: 257 +/-189 Low meat eaters: 298 +/-231 Fish eaters: 230 +/-230	Vegetarian and vegans: 301 +/-169	Regular meat eaters: 256 +/-125 Low meat eaters: 262 +/-146 Fish eaters: 292 +/-151
<b>UK (Bradbury et al.)<sup>43</sup></b>	Male: 270 Female: 263	Vegetarian: 200 Pesco-vegetarians: 217 Low-meat: 192 Regular meat: 165	Male: 359 Female: 369	Vegetarian: 237 Pesco-vegetarians: 232 Low-meat: 179 Regular meat: 170
<b>USA (SDA, Orlich et al.)<sup>58</sup></b>	483.1	Ovo-lacto-vegetarians: 357 Pesco-vegetarians: 400.3 Semi-vegetarian: 343 Non-vegetarians: 298.8	424.1	Ovo-lacto-vegetarians: 347.2 Pesco-vegetarians: 386.0 Semi-vegetarians: 337.0 Non-vegetarians: 319.9
<b>USA, (Robinson-O'Brian et al.)<sup>59</sup></b>	Fruit & vegetables: 5.1 servings per day	Former vegetarians: 3.7 servings per day Never vegetarians: 3.2 servings per day		

### Amendment to the 2006 report

A vegan diet covers micronutrients typically provided by food of plant origin, e.g. magnesium, vitamins C, B<sub>1</sub>, B<sub>6</sub>, folic acid. Fruit and vegetables are among the plant-based sources of these micronutrients. Although vegans in average consume more fruits and vegetables than omnivores, they do not consistently reach the recommended 4-5 portions per day. It is therefore not evident to assume that a vegan diet per se can benefit from the advantages of a diet with a high fruit and vegetable intake, as was emphasized in the previous report.

The variability in fruit and vegetable intakes might need more precise monitoring. Dietary recommendations for vegans should include a reminder to insure an adequate fruit and vegetable intake. This variability also suggests that studies on the association between vegan diets and health outcomes should analyze dietary patterns in vegan diets, and possibly stratify the data by the degree of fulfilment of dietary recommendations.

## 6.2 Micronutrient deficiency risks of a vegan diet

When assessing the micronutrient intake of vegans, care should be taken into recording accurately any supplement intake. A German qualitative study (5 focus groups in different locations with a total of 42 vegan participants) confirms that a minority of vegans do not see the necessity of a supplementation, believing that a well-balanced vegan diet provides all necessary nutrients<sup>31</sup>. Supplements are however recommended by vegan societies, e.g. the Swiss Vegan Society, in particular for vitamin B<sub>12</sub><sup>16</sup>. European studies show that not all vegans follow this recommendation (**table 6-3**).

Estimates in the micronutrient intake are often based on food intake, and do not take into account variations in the bioavailability and absorption rates of each micronutrient. Blood and/or urine samplings are therefore more appropriate as biomarkers for the effective micronutrient status.

Schüpbach et al. show that all diet groups show low intakes / status for some micronutrients. Although the average micronutrient intakes seem to be in the normal reference ranges, with the exception of iron, resp. its biomarker plasma ferritin, the percentage of vegan participants below the cut-offs for deficiencies is critical for selected nutrients (Zn, I, B<sub>2</sub>, B<sub>6</sub>)<sup>38</sup>. This will be discussed in more detail below, together with other potentially critical micronutrients, discussed in alphabetical order.

**Table 6-3: Supplement intake data in different European countries, compared to Swiss recommendations (for healthy adults)**

	<b>Aggregated FCN/SSN recommendations<sup>52,53</sup></b>	<b>Switzerland<sup>38</sup></b>	<b>Denmark<sup>40</sup></b>	<b>UK<sup>42 *</sup></b>	<b>UK<sup>60</sup></b>	<b>Finland<sup>45</sup></b>	<b>Belgium<sup>44</sup></b>
<b>Participants</b>	For healthy adults	VGT n=43 VG n=43	VG m n=33 VG f n=37	VG m n=269 VG f n=534	N= 23	VG m n=6 VG f n=16	VG n=104
<b>Supplements</b>	Recommended for vegans	43% of the recruited participants habitually consumed supplements, and had to interrupt supplementation 14 days before study.	65.7% any supplement	VG m: 60% any supplement 51% any supplement with vitamin B <sub>12</sub> 22.1% Vit B <sub>12</sub> VG f: 67% any supplement 50% any supplement with vitamin B <sub>12</sub> 20% vitamin B <sub>12</sub>	61% vitamin B <sub>12</sub>	91% any supplement 73% vitamin B <sub>12</sub> 68% vitamin D 27% calcium	Not asked

\*data unclear, possible multiple supplementation  
VGT: vegetarian; VG: vegan; m: male; f: female.

## Calcium

In omnivore resp. lactovegetarian diets, milk and dairy products often represent a major dietary source for calcium. Well-planned vegan diets can include sufficient calcium-rich sources, such as green vegetables, nuts and pulses, some mineral waters, and/or calcium-enriched products. Most studies compared actual intake data to the recommended intake of 800 mg. The DACH reference value for adults was increased to 1000 mg Ca<sup>52</sup> suggesting that for many vegans a dietary adjustment / supplementation is necessary.

Some typical examples of naturally calcium-rich food items would be: broccoli (93 mg/100 g), sesame seed (940 mg/100 g), generic mineral water (up to 50 mg/100 ml), pulses, e.g. lentils (57 mg/100 g dry product), dry soybeans (200 mg/100 g)<sup>61</sup>. The Schüpbach et al. study shows that 54% of the vegan participants consumed less than 800 mg Ca/day, whereas only 17% of the vegetarians and 28% of the omnivores did not reach this intake target. The mean Ca intake for the vegan participants was however of 817 mg/day (+/- 285), thus demonstrating that some vegan diets provide an adequate calcium intake<sup>38</sup>. Similar results are reported in the Belgian study, with a mean intake of 730 mg Ca/day<sup>44</sup>; the Finland study reports a mean of 1'004 mg Ca/day for the vegan population, which is only slightly lower compared to the matched non-vegetarian group, with 1'117 mg Ca<sup>45</sup>.

The EPIC cohort was investigated by different groups (for detail refer **to appendix II**). Sobiecki et al. reported in 2016 an adjusted mean calculated intake of 848 mg Ca in the vegan group, with 17.1% of female participants, and 13.5% of male participants not achieving the estimated average requirements<sup>42</sup>. Appleby et al. reported earlier (2007) their investigation on diet and fracture risk<sup>62</sup>. The baseline characteristics showed a mean calcium intake for male: meat-eaters 1'062 mg (+/-325), fish-eaters 1'086 mg (+/-355), vegetarians 1'085 mg (+/-1'085) and vegans 603 mg (+/-232). For women the figures were only slightly lower: meat-eaters 995 mg (+/-303), fish-eaters 1'029 mg (+/-337), vegetarians 1'018 mg (+/-357) and vegans 586 mg (+/-226). The pooled intake of men and women was below 525 mg for 44.5% of the subjects, possibly associated with an increased fracture risk (see chapter 8.6.1).

A second concern is the bioavailability of these calcium sources, considering that vegetables and pulses also contain variable quantities of calcium-binding organic acids (such as phytic and oxalic acid). As there is a lack of food composition data, it could be helpful to plan a calcium-rich diet, preferring food items with lower phytic or oxalic acid contents.

The importance of an adequate calcium intake in children is discussed in chapter 7.2. A long-term calcium deficiency could affect bone health; however, a vegan diet could possibly also include bone-protecting components. The impact of a vegan diet on bone health is discussed in chapter 7.3.

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### Amendment to the 2006 report

The European studies now provide more specific data on the calcium intake and show that calcium intake in vegan diets is lower than other diets, but that intakes of 800 mg can be achieved in average. Attaining a target of 1000 mg requires a well-planned diet, including calcium-rich food sources and water. It should be taken into account that water's hardness (synonymous with calcium content) varies in Switzerland from region to region (c.f. former FCN report).

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### Iodine

Iodine is frequently mentioned as a critical element in vegan diets, e.g. by the German Society of Nutrition<sup>9</sup>. The situation in Switzerland is different, as without the fortification of salt, iodine deficiency would be endemic for the whole population. The fortification of salt has helped fulfilling the population target intake levels (150 µg / d)<sup>63</sup>. The iodine status is regularly monitored. Results of iodine monitoring campaigns up to 2009 led to a mandatory increase of the iodine content of iodized salt from 20 to 25 mg/kg in January 2014<sup>64</sup>.

Although iodized salt is the main source of iodine in Swiss diets, its use is not mandatory; the use of uniodized salts (both in industrial foods and/or household salt) is frequent. The recent menuCH survey reports that 69% of the participants use iodized salt in their household<sup>65</sup>, showing a reduction from the 80% recorded in the last iodine monitoring<sup>63</sup>. Chappuis et al. investigated the use of iodized salt in the general Swiss adult population and observed that over a third of the survey participants do not regularly use iodized salt<sup>66</sup>.

Specific data on the use of iodized salt for vegans who cannot rely on sea fish or cow's milk for their iodine supply. Including seaweed in the diet could lead to higher iodine intake<sup>40</sup>; the frequency in use of these algal sources is unknown. No further data was found on the calculated iodine intake in the vegan subjects in the Swiss studies.

Urine iodine values were calculated in the recent study from Schüpbach et al.<sup>38</sup> The median concentrations range from 83 µg/l in omnivores to 75 µg/l in vegetarians (not a significant difference) to a significantly lower 56 µg/l in vegans<sup>38</sup>. In all three dietary groups a majority (≥ 65%) does not reach the cut-off value of 100 µg/l currently recommended by the WHO. Similar trends were observed in the plasma data, with 78.8% of vegans below the cut-off for deficiency.

The iodine status for a larger sample of the Swiss population (n=1481) was assessed during the Swiss survey by Haldimann et al. on salt intake 2010-2012<sup>67</sup>. The median urinary concentration was of overall 75.7 µg/l, thus in a similar range as the results for omnivores (83 µg/l) in the Schüpbach et al. study. The significant difference between women (62.5 µg/l) and men (90.6 µg/l), in the Haldimann et al study, suggests that the vegan data should be analysed for gender differences, in order to assess the potentially higher prevalence of an iodine deficiency in vegan women.

These results show that although iodine supplementation is necessary for the Swiss population, vegans are at higher risk, which could lead to a reduced formation of active thyroid hormones. This however depends not only on a sufficient intake of iodine.

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### Amendment to the 2006 report (and the FCN-iodine report)

Vegans are at particular risk for an iodine deficiency, in particular if they are not regularly using iodized salt. The use of iodized salt in vegan groups should be investigated and if necessary more actively encouraged and monitored. Communication is necessary in order to raise the awareness of possible consequences for certain population groups.

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### Iron

Iron is often mentioned as critical mineral for vegetarians and vegans e.g.<sup>9,68,69</sup>, recommended intakes vary, depending on different institutions, e.g. DACH reference values 10 mg (for males) / 10-15 mg (and for post-resp. premenopausal women).

In a healthy Swiss population<sup>38</sup> the calculated average daily intake of iron was highest in vegans (median 22.9 mg, 12.8-43.0), followed by vegetarians (median 14.7 mg, 7.7-44.3) and omnivores (median 11.8 mg, 7.2-43.3). Iron can be found in plants and in food of animal sources in different forms. Plants contain mainly Fe<sup>3+</sup>, a non-heme iron, with limited bioavailability, unless consumed concomitantly with ascorbic acid-containing food, which reduces this iron to Fe<sup>2+</sup>. Food of plant origin also contains iron in form of phyto-ferritin: e.g. 40-90% of iron in pulses is in this form<sup>70</sup>. Investigations show that this iron form possibly has a good bioavailability, the hypothesis being that it can be taken up by endocytosis, as based on tests with cultured cells<sup>71-75</sup>.

Schüpbach et al further analysed plasma levels for haemoglobin and ferritin. All three groups held the same haemoglobin status (145 -147 g/l +/- 11-14), but different plasma ferritin (PF) levels. Omnivores had the highest median levels (58 µg/l), vegetarians the lowest (32 µg/l), vegans lay between the two other groups (40 µg/l), the data collected from the vegan group were however not statistically different from that of omnivores, resp. vegetarians. The authors claim that for all three groups the plasma ferritin levels lay well within the normal range of 15-300 µg ferritin/ l, without clinical symptoms. The Swiss Medical Board however recommends a cut-off value of 50 µg/l<sup>76</sup>, the Swiss data of the Schüpbach study should be re-analysed in regard to this reference value, in order to have a better estimate of the percentage of participants below this cut-off value.

In the mentioned Belgian study, the calculated intake of iron is the highest in vegans, followed by vegetarians, and with the lowest calculated intake in the omnivore group. The calculations were based on the FFQ and a Belgian FCDB. These results do not take into account the bioavailability of the different forms of iron (Fe<sup>3+</sup>/Fe<sup>2+</sup>/ferritin and /or heme iron), and no blood sampling was performed<sup>44</sup>. The Finnish study also shows a non-significant higher intake of iron in the vegan group (21 mg +/-9 vs. 15 mg +/-7 in the non-vegetarian), the median ferritin levels in serum were however lower (26 µg/l vs 72 µg/l), both in the reference range, even when stratified (male/female)<sup>45</sup>.

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## Amendment to the 2006 report

The recent European studies confirm that the calculated iron intake is frequently higher in vegans than with other diets, due to the high content of  $\text{Fe}^{3+}$  in food of plant origin. Depending on the source its absorption varies; more research is needed to clarify the bioavailability of phyto-ferritin.

The Swiss study highlights the importance of measuring plasma ferritin, and not only haemoglobin as a biomarker, taking into account the recommendations of the Swiss Medical Board.

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## Long-chain polyunsaturated n-3 fatty acids

Very-long chain polyunsaturated n-3 fatty acids ( $\text{C}_{20}\text{-C}_{22}$ ) such as eicosapentaenoic acid (EPA,  $\text{C}_{20:5}$ ) and docosahexaenoic acid (DHA,  $\text{C}_{22:6}$ ) are important constituents of cell membrane lipids; in particular, DHA is enriched in brain lipids and in the photosensitive rod inner membranes of the eye. EPA is a precursor for several series of bioactive molecules, participating among other functions in blood clotting, inflammatory processes, secretory activities. Very low DHA levels are associated with depression and neurological disturbances<sup>77</sup>. Specific aspects of the essentiality of EPA and DHA during neurological development of the fetus and after birth are discussed in chapter 7.2.

Omnivores, pescetarians and (ovo-)lactovegetarians have a supply of EPA and DHA in their diet; e.g. fatty fish is a good nutritional source for DHA.

In most studies, intake estimates are aggregated for all polyunsaturated fatty acids<sup>40,42,44,45</sup>. These studies show slightly higher PUFA intakes for vegan than omnivores (values, adjusted for age and sex, vary among the studies: vegans 21-26 g PUFA, omnivores 15-22 g PUFA). The specific intake of n-3 fatty acids is not calculated in these studies. One Australian study shows that vegans have an intake of 84 mg n-3 fatty acids / day, whereas omnivores had an intake of 216 mg<sup>78</sup>. Sanders reviews older literature and mentions intakes of ALA 2.2 g/day for vegans and 1.3 g for omnivores<sup>79</sup>.

Vegans show very low levels of DHA in their circulating lipids, but not lower than omnivores who have a limited intake of DHA+EPA<sup>80</sup>. Some authors prefer measuring the erythrocyte fatty acid composition (e.g. an Omega 3-Index) as an indicator for long-term intake of long-chain PUFAs<sup>60</sup> as a potential biomarker for CHD risk, this approach has yet to be validated<sup>81,82</sup>.

Low dose EPA+DHA-supplements can markedly elevate the blood DHA and EPA levels<sup>79</sup>. A supplementation is of particular important in life stages with higher requirements, such as pregnancy, lactation, or childhood<sup>83</sup>. Chapter 7 will cover these aspects in more detail.

As some algae build directly DHA, vegan DHA supplements are available. Vegetarians and vegans should also prefer ALA-rich oils instead of oils rich in linoleic acid. Good ALA sources are rapeseed (canola) oil and walnuts; other ALA-rich oils, such as flaxseed, walnut and chia oils are very prone to oxidation reactions.

Humans are able to elongate and desaturate  $\alpha$ -linolenic acid (ALA,  $\text{C}_{18:3}$ ), an essential n-3-precursor fatty acid, to EPA and, to a minor extent, to DHA. Linoleic acid (n-6) competes with ALA for the enzyme binding sites. Since normally the amount of linoleic acid in the diet exceeds by far the amount of ALA, the formation of EPA and DHA stays very modest in comparison to the formation of arachidonic acid, the n-6 compound corresponding to EPA. The endogenous conversion of ALA to EPA and DHA is limited, but evidence suggests that it might be sufficient to lead to stable DHA and EPA levels in vegans over many years. This process is dependent on metabolic genetics, age (decline with age), sex (less conversion in young males), health status (chronic disease, smoking), and dietary composition<sup>84</sup>.

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## Amendment to the 2006 report

Recent publications confirm the conclusions of the 2006 report: a sufficient intake of n-3 fatty acids in vegan diets can be critical, and needs to be covered by choosing ALA-rich oils or ALA-rich nuts, as well as DHA-rich algal extracts, in particular during specific life stages (pregnancy, breast-feeding, childhood).

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## Selenium

The DACH recommended intake for selenium is of 70 (m)/60 (f) µg/d. It is an essential trace element with functions as seleno-cystein in the active centre of several important enzymes. The antioxidant capacity depends amongst others on Se-containing peroxidases and thioreductases. The formation of functional thyroid hormone T3 depends on deiodinases, which are also selenoproteins. Today many human selenoproteins have been identified, but their functions are still not fully elucidated. Deficiencies in selenium supply induce health problems concerning the muscles, the heart and the immune system<sup>85</sup>. The existing data on low selenium status and colorectal cancer risks in vegetarians are non-conclusive<sup>86,87</sup>.

European soils contain less selenium than e.g. North American soils, as previously reported by Zimmerli<sup>88</sup>. More recent research warns that climatic changes could exacerbate the problem of selenium depletion<sup>89</sup>. Imported cereals therefore often cover selenium needs. Choosing regionally and organically grown cereals (e.g. without a specific selenium-containing fertilizer) could lead to decreased selenium intake, even for omnivores.

There are already some concerns about a generalized suboptimal selenium status in Europe<sup>90</sup>. Data are missing on calculated dietary intakes, however the selenium status in blood is regularly monitored in Switzerland, with the most recent monitoring concluding that with an “overall mean serum concentration of 98 µg/l (n=1’847), the selenium status of the healthy adults can be assessed as adequate”<sup>91</sup>. Recent analysis has confirmed that the intake of selenium corresponds directly to the plasma levels<sup>92</sup>. Data on the selenium plasma levels in vegetarian or vegan population groups in Switzerland are scarce. The most recent study by Schüpbach et al. found no relevant differences in serum selenium concentrations between omnivores, vegetarians and vegans, with values between 90 and 94 µg/l, the vegan had the greatest variability, 90 µg/l +/-21.9, suggesting that some vegans are at the lowest end of the recommended range of 70-150 µg/l<sup>38</sup>.

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## Amendment to the 2006 report

In the previous report, vegans were considered at being at risk of a selenium deficiency; this could still be the case for some vegans, as the Schüpbach et al study shows.

Selenium monitoring should include questions on the dietary habits. Further investigations are also necessary to assess whether there is an accentuated risk of a selenium deficiency in Switzerland for specific populations groups who consume mainly regionally and organically grown plant products, independently of their dietary choices.

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## Vitamin B<sub>12</sub>

The DACH recommended intake for vitamin B<sub>12</sub> is 3 µg/d (for the general adult population). Vitamin B<sub>12</sub> is synthesized by some bacteria and is bio-accumulated along the food chain, supplementation with either cobalt (ruminants) or vitamin B<sub>12</sub> (non-ruminants) is common in animal husbandry<sup>93</sup>. In an omnivore diet meat from ruminants, is a good source for this vitamin (e.g. 2 µg/100 g beef filet). Minor sources of vitamin B<sub>12</sub> are fermented products, in particular dairy products (e.g. 2 µg/100 g Gruyère-type cheese, 0.5 µg/100



g yoghurt); all data from the Swiss FCDB; a detailed overview of vitamin B<sub>12</sub> content of different meat types is provided by Gille & Schmid<sup>94</sup>. Fermented plant-based food (e.g. sauerkraut, tempeh) contain traces of vitamin B<sub>12</sub><sup>95</sup>; precise data for products on the Swiss market are however missing.

Other possible vegan sources of vitamin B<sub>12</sub> exist, e.g. Chlorella algae containing 3.9 -11.4 ng cyano-cobalamin/30 g algae, these quantities are however extremely low<sup>96</sup>. Purple laver (nori) and some mushrooms have also been mentioned as possible active vitamin B<sub>12</sub> sources<sup>97</sup>. These are not necessarily frequent items in Western diets; for more data, they should be included in vegan-appropriate FFQs and reliable reference composition data are needed.

The uptake of this vitamin in the human body is mainly possible with the assistance of transport proteins, salivary R proteins, followed by the intrinsic factor (IF) produced by the stomach mucosa. Active absorption occurs in the distal part (ileum) of the gut, and is probably limited to 1.5-2 µg/meal<sup>95</sup>; furthermore, the absorption capacity decreases with age. The main cause for decreased absorption is an impaired secretion of gastric acid and IF due to mucosal inflammation, e.g. as a consequence of a long-term intake of proton-pump inhibitors. Mucosal inflammation becomes more prevalent with age (atrophic gastritis), leading to a decreased release of cobalamins from the proteins due to impaired protein denaturation and therefore decreased absorption. These aspects must be considered when assessing vitamin B<sub>12</sub> intake as the calculated intake, based on dietary assessments and FCDM alone could overestimate the effectively absorbed amount.

**Table 6-4** reports results of the studies comparing the calculated dietary intake (excluding supplements) with an estimated average requirement (EAR) of 2 µg/day showing that this requirement is not reached by vegans. This EAR is below the D-A-CH reference value of 3 µg for healthy adults<sup>52</sup>, as well as below the adequate intake (AI) of 4 µg proposed by the European Food Safety Authority<sup>98</sup>.

Serum B<sub>12</sub> is traditionally used as a biomarker for bioavailable B<sub>12</sub> (from dietary intake and / or depletion of the hepatic store) and has been used to assess the vitamin status in vegetarians. A review of the literature up to 2012 shows that vegans are at higher risk of a vitamin B<sub>12</sub> deficiency. More than 50% of the participants had serum values below the cut-off range of 120-180 pmol/l<sup>99</sup>. The Finnish study reports high median serum values of 328 pmol/l for vegans, 508 pmol/l for non-vegetarians<sup>45</sup>. The Swiss study is more difficult to evaluate, 43% of the participants were taking supplements up to 14 days before the study and had serum values of 342 pmol/l, those without supplementation had a high median value of 274 pmol/l. Only 7.5% of the vegan participants showed a deficiency. The authors conclude that the B<sub>12</sub> status thus measured does not reflect the possibility of depletion of the body storages<sup>38</sup>. Lacking awareness of the slow depletion of vitamin B<sub>12</sub> stores could also be a factor leading to the denial of the necessity of a supplementation; indeed, high serum B<sub>12</sub> values in the initial vegan phase can be erroneously used as proof that a supplementation is not necessary.

Serum B<sub>12</sub> is therefore not the only biomarker, which should be taken into consideration<sup>95,100-102</sup>. table 6-5 lists other markers recommended by these authors, with holo-transcobalamin II being the most frequently recommended analysis. A higher folic acid intake (typical of a vegan diet) could mask vitamin B<sub>12</sub> deficiency symptoms if only a macrocytic anemia is being searched for.



**Table 6-4: Calculated average dietary intake of vitamin B<sub>12</sub>**

Study	Supplementation	Vegan diet (µg)	Vegetarian diet (µg)	Omnivorous diet (µg)
Finland <sup>45</sup>	Excluded	0.9 (+/-0.8)	-	8.7 (+/-5.6)
Switzerland <sup>38</sup>	Excluded, or interrupted days before the study	140.2 (0-6.4)	1.6 (0.3-14.4)	4.1 (0.9-14.7)
UK, dietary intake only (without supplements) <sup>42</sup>		Male: 0.7 (+/-0.71) Female 0.68 (+/-0.56)	Male: 3.11 (+/-2.02) Female: 2.96 (+/-1.84)	Male: 8.24 (+/-3.1) Female: 7.85 (+/-3.04)
Denmark <sup>40</sup>		Male: • 0 (from diet) • 10 (mean, incl. supplements) Female: • 0 (from diet) • 25 (mean, incl. supplements)		Male: 6.1 (4.8-7.7) Female: 4.2 (3.3-5.3)

Vitamin B<sub>12</sub> supplementation is highly recommended for all vegans<sup>16</sup>, this recommendation is not followed by all, as **table 6-3** shows. Anecdotal evidence points to a certain resistance, so called “chemophobia” to supplements produced by biotechnological methods<sup>103</sup>. Whilst this does not seem to be the case in the majority of vegans, this is often true for the smaller sub-population of vegans, e.g. raw vegans, and Rastafarian vegans (who eschew both preservatives and vitamin supplementation).

**Table 6-5: Blood Biomarkers for the assessment of the vitamin B<sub>12</sub> status**

Biomarker	Comments	Reference for normal value
Total serum B <sub>12</sub>		<150 pmol/l very probable deficiency 150-300 pmol/l: grey area >300 pmol / l; deficiency not probable <sup>104</sup>
Holo-Transcobalamin II (holoTCII)	Marker for B <sub>12</sub> depletion, resp. for active B <sub>12</sub> . It can be used as a screening instrument, is not recommended in case of kidney insufficiency	>35 pmol/l
Methylmalonic acid (MMA) in serum	Methylmalonic acid reflects vitamin B <sub>12</sub> metabolism; elevated values are therefore linked to a vitamin B <sub>12</sub> deficiency. This test has a lower specificity in older adults	<270 nmol/l
Methylmalonic acid (MMA) in urine	See above, spot urine is sufficient	< 3.6 mmol MMA/mol creatinine
Homocystein in serum		<10µmol / l
Mean corpuscular volume of erythrocytes	can be masked by iron deficiency or high intake of folate	

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## Amendment to the 2006 report

In the previous report the risk of a vitamin B<sub>12</sub> deficiency was not considered as being high, under the assumption that supplementation was widespread.

The recent European reports show however that not all vegans comply with this recommendation, with a small percentage (7.5%) of the Swiss Schüpbach sample showing a deficiency. However, the specific recruitment criteria mean that the participants of this study were not representative for their supplement use. Further investigation on supplement intake is necessary, as well as more efforts in recommending vitamin B<sub>12</sub> supplementation and/or fortification of food (e.g. of protein rich food components).- see chapter 7.2.

More nutrient data on fermented food items typically consumed by vegans (vegetable or soy-based products, e.g. "soy-based"-yoghurt products) should be made available.

As a biomarker holo-transcobalamin II has emerged as a reliable indicator for vitamin B<sub>12</sub> depletion, together with serum or urine MMA. A regular monitoring is necessary, in particular for critical populations groups, e.g. children, pregnant women (see chapter 7).

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## Zinc

The DACH recommended intake for zinc is 10 mg/d (males) and 7 mg/d (females). This element is frequently mentioned as a critical element for vegetarians and vegans<sup>105</sup>. It is a very important trace element with multiple functions in the human body. It is needed as cofactor in several hundred enzymes and proteins, participates in transcription and translation processes, thus influences growth, the secretion of hormones, the formation and growth of bones and stimulates responses of the immune system<sup>106</sup>. Zinc is found mainly in protein-rich food, both of animal and plant origin. As some vegans may consume less protein than recommended (see **table 6-1**), their zinc intake could be lower; furthermore, the bioavailability of zinc has to be taken into account. A comparative meta-analysis concluded that zinc intake and serum zinc levels are lower in populations following vegetarian diets, stressing that the variability of vegetarian diets made comparisons difficult<sup>107</sup>. In further analyses, the vegan groups had the lowest zinc serum values and zinc intakes<sup>108</sup>. The adjusted calculated mean zinc intake in the EPIC study was also significantly lower in the vegan group (8.7 mg) than in the vegetarian group (10.3 mg) and in the meat-eating group (10.5 mg)<sup>42</sup>. In an Australian study with young woman (n=308), micronutrient intake was assessed by FFQ, using the Australian FCDB. Participants were classified according to their avoidance of specific animal-derived products, "non-avoiders" could be considered omnivores (with a zinc intake of 15 mg, SD of 5), "avoiders of all" could be considered vegans (with a significantly lower zinc intake of 12 mg, SD 3)<sup>78</sup>. The higher Australian values lead to the question whether Australian products are naturally higher in zinc, making comparisons difficult.

In the Swiss study<sup>38</sup>, the average daily intake of zinc was comparable in all three-diet groups and well above the estimated average requirement (EAR) for this element. However, the blood levels differed significantly for each group with the highest level in omnivores, followed by the vegetarians and the lowest level in vegans. Consequently, 47% of the vegan subjects had blood levels below the cut-off values (74 µg / dl for men, 70 µg / dl for women). In the vegetarian group this was the case for 19% and in the omnivorous group for 11% of the participants, the difference between the vegetarian and omnivorous groups is not significant<sup>38</sup>.

These results show that calculated zinc intakes, based on FFQ and generic zinc contents of food items do not reflect the bioavailability of zinc and confirm the risk of zinc deficiency in vegan diets. This is of concern for all age groups, in particular however in infancy, childhood, pregnancy and breastfeeding, where physiological demands are higher. These issues are discussed in chapter 7.

Saunders et al point out that a major factor affecting zinc bioavailability is phytic acid, and suggests processing food in order to decrease the phytic acid / phytate content (e.g. enzymatically) or zinc supplementation<sup>105</sup>. A molar ratio phytic acid: zinc of > 15 is considered to decrease the bioavailability of dietary zinc<sup>109</sup>.

Unfortunately neither the Swiss FCDB, nor the frequently cited German FCDB (Bundes Lebensmittelschlüssel, BLS) lists phytic acid content<sup>61</sup>. Some data were found in the “Souci” database and are summarized below (**table 6-6**). If this data is correct, in many food items of plant origin the phytic acid: zinc ratio is > 15. No further data were found for a wider selection of pulses, soy products and other typical plant-based protein sources<sup>110</sup>.

Zinc deficiency is also widespread in low-income countries, a Swiss study shows that specific treatment of cereals, e.g. the enzymatic dephytinization of oats, leads to an increase of the bioavailability of zinc. The same authors demonstrate the benefits of a zinc fortification<sup>111</sup>.

**Table 6-6: Content of zinc and phytic acid in selected food items (values per 100g edible portion)<sup>110</sup>**

Product categories	Product	Zinc [mg]	Phytic acid (PA) mg	Molar ratio PA zinc
<b>Cereals</b>	Maize, whole grain	1.7	940	55
	Quinoa	2.5	541	21
	Rice unpolished	1.6	890	55
	Rice polished	1.1	240	23
	Rye	2.9	878	33
	Wheat	2.6	878	33
	Wheat germ	18	1470	8
<b>Legumes</b>	Bean	2.5	800	32
	Chick pea	1.4	280	20
	Soya bean	4.2	1250	29
	Mung bean	2.1	629	29
<b>Nuts</b>	Peanut	2.8	1336	47

## Amendment to the 2006 report

The recent studies confirm that an omnivorous and a vegetarian diet provide comparable zinc intakes.

These studies show that a vegan diet leads to lower zinc blood levels, which for 47% of the participants of the Swiss study were below the cut-off value. This indicates that communication is needed on good vegan sources for zinc. Research on the ideal processing resp. cooking of zinc-containing raw materials and the improvement of the zinc bioavailability should be encouraged.

## 6.3 Further risks of vegan diets

Dietary shifts towards more food of plant origin could lead to shifts in the exposition of specific food-associated contaminants. The exposition to methylmercury, dioxins, polychlorinated biphenyls etc., typically accumulated in fatty foods of animal origin, is expected to be lower in a vegan or vegetarian diet; whereas a higher exposition is expected to typical contaminants in food of plant origin, e.g. arsenic in rice products, specific pesticides, cadmium. For arsenic, no Swiss data were found related to dietary patterns, but Japanese data indicate that rice-based products, which would typically be part of a vegan diet, could be contaminated with arsenic<sup>112</sup>. Monitoring of dietary arsenic in Switzerland has now become necessary, due to the introduction of cut-off values for arsenic with the Swiss food legislation reform in 2017<sup>113</sup>.

Van Audenhaege et al show that a vegan diet could lead to an increased exposure to specific pesticide residues in France (tri-allate, and organophosphates (OPs) such as chlorpyrifos-methyl and diazinon)<sup>57</sup>.

Berman et al measured urinary levels of pesticides in individuals, stratified by different dietary patterns in the vegetarian and vegan Jewish Amirim community in Northern Israel<sup>114</sup>. Focus was made on OPs and carbamates, which are widely used in the Israeli agriculture. Dietary exposure was measured by the excreted metabolites of these pesticides. Higher values were found, when comparing the Amirim sample of to those of a wider Israeli Jewish sample. These values were found to be associated with the higher intake of

fruit (25% of the caloric intake, compared to 6% for the reference group) and vegetables (31% of the caloric intake, compared to 10% for the reference group). When organic produce was preferred, lower values for excreted OP metabolites were observed. This study has some limitations for its use in comparison with other data, in particular for the data on fruit and vegetable consumption, e.g. the classification of food items.

In conclusion, the data from France and Israel show that patterns in pesticide residues depend on the dietary patterns. OP-levels could be monitored in connection with a vegan/vegetarian diet. Furthermore, the extent of consumption of organic produce could also be relevant, and could be assessed in case of a monitoring.

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## Conclusion chapters 5-6

Data from Switzerland and other countries show that a vegan diet, when carefully planned to cover energy and macronutrient needs and mandatorily combined with supplements/ fortified food, can be comparable, from a purely nutrient perspective, to other dietary forms, at least for healthy adults.

The data show however that this ideal well-planned diet is not always followed; this has been shown with data on fruits and vegetable consumption resulting in very wide ranges in macronutrient and micronutrient intakes. All these studies are based on small numbers of participants (with a possible selection bias), with different inclusion criteria of diets, different duration and adherence to a specific diet.

Based on these data, there is no evidence for the position stated in the previous report, that vegan diets are healthy diets, mainly due to the high intake of fruit and vegetables. Possible risks associated with a higher intake of plant-based food (e.g. arsenic or pesticides) need further investigation.

Mandatory supplementation for vitamin B<sub>12</sub> should be enforced, as well as emphasis on the specific higher risk of iodine deficiency, if the general recommendation for iodized salt is not followed. Information about good sources for iron, zinc, calcium and n-3 fatty acids should be provided (food and/or supplements, and/or fortified food), as well as the consequences of selenium deficiency (in particular in relation to the geographical differences in soil selenium depletion).

This communication should particularly target groups who chose a vegan diet for ethical- rather than those who follow this diet for primary health reasons (the minority). Monitoring of critical micronutrients is highly recommended.

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# 7 Life cycle aspects of vegan diets

## 7.1 Pregnancy and breastfeeding

**Lead author: Katharina Quack Lötscher**

The impact of a vegan diet during pregnancy and in the pre-conceptional phase is still a little-researched topic, specific case-reports, cross-sectional data, and prospective longitudinal data are still lacking. Older data are summarized by Cofnas, showing that nutrient deficiencies during pregnancy could be potentially harmful for the foetus<sup>115</sup>.

Therefore, individual medical and dietetic counselling is highly recommended for women desiring to follow a strict vegan diet during pregnancy and lactation<sup>115,116</sup>. The reasons and motivation for a plant-based diet should be evaluated; as seen in the previous chapter. Piccoli et al. found in their narrative review that only iron and vitamin B<sub>12</sub> could be critical in some vegan or vegetarian diets<sup>117</sup>, particularly when the increased needs for iron and vitamin B<sub>12</sub> supplementation are not taken into account.

Pistollato et al. reviewed the existing literature and summarize further possible issues related to maternal plant-based dietary patterns. Main issues these authors are the lower intake of n-3 PUFAs (with possible

negative outcomes for children), lower B<sub>12</sub> intake, lower mineral intake (iron, zinc, iodine and calcium), as well as vitamin D deficiencies<sup>118</sup>.

As seen in chapter 6.2, the source of iron in a vegan diet can influence absorption rates, leading to variable hemoglobin and ferritin levels for vegans. An iron deficiency can lead to anemia. In Switzerland, it is recommended to test hemoglobin and ferritin at the beginning of pregnancy in all women before treating them for anemia or iron deficiency, independently of their dietary choices<sup>119</sup>. Vitamin B<sub>12</sub> should be tested for women following a vegetarian or vegan diet: starting with vitamin B<sub>12</sub> in serum, followed, in case of deficiency (or near-deficiency), by HoloTCII and MMA testing, and supplemented according to results<sup>120</sup>. Supplementation should be continued into the lactation phase.

A vegan diet can lead to a higher intake of phytoestrogens (contained e.g. in soy-based products, linseed), with conflicting data on the possible risk of hypospadias, i.e. abnormal location of the urinal opening in the penis<sup>118,121</sup>, further studies are needed to confirm this hypothesis.

Independently of the diet form, vitamin D supplementation (600 IU/day) is recommended for all pregnant women<sup>122</sup>.

Pregnant and lactating vegetarian women who avoid seafood and algae and live in an area where the soil is deficient in iodine may have insufficient iodine intake to meet the needs of the fetus and the breastfed baby, with hypothyroidism as a consequence. The FCN report on iodine stated that a mild to moderate iodine deficiency is prevalent among pregnant and lactating women in Switzerland, because iodine needs increase to a minimum of 250 µg<sup>63</sup>, this corresponds to the “DACH reference values of 230 µg (pregnancy) to 260 µg (while breastfeeding)”<sup>52</sup>. Consequently, the FCN recommended all pregnant and lactating women to use iodized table salts available in Switzerland. The 2016 iodine survey for Switzerland shows a decrease in the urinary iodine concentration in pregnant women from 162 µg/l in 2009 to 140 µg/l in 2015 despite an increase in iodine concentration in salt in 2014<sup>123</sup>. Therefore, a separate supplementation, besides iodized table salt, with 150 µg should be considered. Otherwise, deficiencies are likely, with important consequences for the development of children.

The zinc status during pregnancy has been object of a review and meta-analysis, comparing vegetarian to non-vegetarian (omnivore) women, but not specifically vegan women. Not only intake estimates, but also several biomarkers were used (serum/plasma, urine, hair samples). Most studies showed that the zinc status was lower in the vegetarian groups than in the non-vegetarian (omnivore) groups; both were however below the recommended levels<sup>52</sup>.

A vegan diet is not recommended during pregnancy according to general dietary recommendations by one of the standard references in the German-speaking area, Koletzko et al.<sup>116</sup>. However, if a vegan diet is strongly desired by the pregnant woman, specific blood analysis, based on an individual dietary assessment, followed by medical and nutritional counselling and supplementation are necessary, taking into account the generally recognized target nutrient intakes for pregnancy and lactation<sup>124</sup>.

Progress in the general physiological understanding of nutrient needs during pregnancy (e.g. iodine reference values) has to be taken into account and included in dietary guidelines for pregnancy<sup>124</sup>.

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### **Amendment to the 2006 report**

The recent reviews confirm previous recommendations, however research in this field is still scarce, and collecting more data is highly recommended. Pregnancy is linked with increased nutrient needs, with iron, iodine, zinc and vitamin D being critical, as well as selenium. Iron deficiency should be monitored and accordingly supplemented.

Vegans should in addition monitor their vitamin B<sub>12</sub> status and in any case use supplements for this vitamin.

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## 7.2 Infants / children

**Lead authors: Oswald Hasselmann, Pascal Müller**

Little is known about the prevalence of infants and children fed on a vegan diet in Switzerland. In a large German nutritional survey (KiGGS-Study) only 1.7% of boys and 3.2% of girls older than 3 years reported being on a vegetarian diet<sup>125</sup>, no information is available about children on an exclusively vegan diet.

When choosing a particular diet for a child, caregivers should be aware that the consumed food will form the basis for the rapidly developing biological organism.

This development is not only reflected in growth and weight gaining but on a much smaller scale in synaptogenesis within the central nervous system, specific gene activation or silencing, immune competence, allergy predisposition, even emotions and cognitive potential are influenced by the choice for and the quality of the food consumed<sup>126</sup>. The type of early nutrition has furthermore an influence on feeding preferences when becoming an adult<sup>127</sup>. When parents / caregivers decide on a vegan diet for their young children, they depart from well-established feeding patterns and assume thereby the whole responsibility of providing an adequate nutrition for their children. We do not know of any study conducted to investigate possible long-term health benefit of a well-planned vegan diet started in pediatric age. Due to the limited data on the impact of vegetarian diets in childhood, it is therefore difficult to draw conclusions on health benefits or risks of these diets<sup>128,129</sup>. More is known about particular aspects within a vegan diet such as energy supply, protein composition, and supply of long chain fatty acids, iron, zinc, vitamin D, iodine, calcium and vitamin B<sub>12</sub>. In the following sub-chapters, emphasis will be laid on the expected effects if the age dependent minimum requirements for a child cannot be met. The knowledge about these potential shortcomings should form the basis for a preventative substitution of missing nutrients or adaption of the vegan diet.

Plant proteins have a lower digestibility and a more limited amino acid composition than animal derived proteins. Therefore, their intake has to be increased by 30-35% for children up to the age of two years, by 20-30% for two to six year olds and by 15-20% for those older than six years of age to meet the required level<sup>130</sup>. This will translate into an additional 2-14 g of protein per day. Children have higher requirements for essential amino acids, according to the 2007 WHO/FAO/UNU report<sup>131</sup>.

To ensure a complete and sufficient essential amino acid supply, a well-planned mixture of different plant-derived proteins (e.g. cereals, nuts, seeds, fruits, legumes and vegetables) should be provided within 24 hours. Due to the higher bulk volume of plant protein in relation to gastral filling capacity, a premature feeling of satiety could lead to a possible energy deficit. Food with concentrated calories and nutrients such as mashed tofu or avocado, bean spreads and cooked dried fruits could be used in such a situation.

If an infant cannot be breastfed, the only adequate vegan alternative is a soy-based methionine-fortified infant formula, as recommended by the ESPGHAN Committee on Nutrition<sup>132,133</sup>. There are no commercial formula options that do not contain animal products for those infants, who are intolerant to soy formula. Moreover, compared to infant formulas based on cow's milk, soy-based formulas have a higher concentration of phytate, aluminum, and phytoestrogens (isoflavones) which might have detrimental effects for the infant, unless these formulas have been specifically pretreated to decrease the concentration of these substances. A recent systematic review concluded that modern soy-based infant formulas were safe regarding growth and bone health as well as metabolic, reproductive, endocrine, immune and neurological functions<sup>134</sup>. Omega-3 fatty acids such as  $\alpha$ -linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) are essential for neurological development (e.g. synaptogenesis, retina development). As DHA and EPA are abundant in seafood and algae, a child not receiving these foods can only rely on precursors of DHA and EPA such as linolenic acid, which can be found in e.g. flaxseed, walnuts, rapeseed, chia<sup>6,84</sup>. Preterm children are at a higher risk of developing a deficiency in these nutrients, as their capacity to convert precursors is probably limited. Supplementation with long-chain n-3 fatty acids could be considered, more research is needed.

Table 7-1 Amino acid scoring patterns for toddlers, children, adolescents and adults <sup>131</sup>

Abbreviations for essential Amino-Acids*			His	Ile	Leu	Lys	SAA	AAA	Thr	Trp	Val
Tissue amino acid pattern (mg/g protein)			27	35	75	73	35	73	42	12	49
Maintenance amino acid pattern (mg/g protein)			15	30	59	45	22	38	23	6	39
Protein requirements (g/kg/d)											
Age (yr)	Maintenance	Growth	Amino acid requirement (mg/kg/d)								
0.5	0.66	0.46	22	36	73	63	31	59	35	9.5	48
1-2	0.66	0.20	15	27	54	44	22	40	24	6	36
3-10	0.66	0.07	12	22	44	35	17	30	18	4.8	29
11-14	0.66	0.07	12	22	44	35	17	30	18	4.8	29
15-18	0.66	0.04	11	21	42	33	16	28	17	4.4	28
>18	0.66	0.00	10	20	39	30	15	25	15	4.0	26
			Scoring pattern mg/g protein requirement								
0.5			20	32	66	57	27	52	31	8.5	43
1-2			18	31	63	52	25	46	27	7	41
3-10			16	30	61	48	23	41	25	6.6	40
11-14			16	30	61	48	23	41	25	6.6	40
15-18			16	30	60	47	23	40	24	6.3	40
>18			15	30	59	45	22	38	23	6.0	39

\*His, histidine; Ile, isoleucine; Leu, leucine; SAA, sulphur amino acids; AAA, aromatic amino acids; Thr, threonine; Trp, tryptophane; Val, valine.

**Iron** has an important role in hemoglobin synthesis, nerve myelination, neurotransmitter synthesis, and hippocampal energy metabolism. Iron requirements are higher during infant and adolescent growth spurts. Iron deficiency can contribute to anemia and more rarely to atrophic gastritis, which can lead to a decreased production of the intrinsic factor, which is necessary for vitamin B<sub>12</sub> absorption. Children low on iron seem to score lower in developmental screening tests<sup>135</sup>. As mentioned in chapter 6, phytates, abundant in plant products, inhibit non-heme iron as well as zinc absorption by forming insoluble complexes in the gastrointestinal tract. Iron from non-meat sources has due to its high content of phytates, dietary fibers and tannins a lower bioavailability. As long as our knowledge about phytoferritin is still limited children fed on a vegan diet should increase their iron intake by about 1.8 times, compared to those fed on animal products<sup>136</sup>. Sufficient amount of vitamin C rich food can partly compensate for this decreased bioavailability of iron by reducing Fe<sup>3+</sup> to the more soluble Fe<sup>2+</sup>.

If **zinc** is not provided by animal products, it has to be supplied from fermented soy products (e.g. miso, tempeh), seeds and nuts<sup>6</sup>. As vegetarians and vegans have a high intake of phytates and polyphenols, zinc absorption is often diminished. However, data on zinc serum concentrations are sparse and difficult to correlate with dietary intake. Clinical signs of deficiency are rare among vegetarian and vegan children<sup>137</sup>. According to the International Zinc Nutrition Consultative Group (IZiNCG), zinc should be supplemented (5 mg Zn/day for children aged 6–36 months, 10 mg Zn/day for older children) in case of a low dietary intake<sup>138</sup>.

**Vitamin D** can be produced endogenously via skin exposure to ultraviolet light. However, the recommended minimum of 30 min/D on uncovered arms without applied sun screen<sup>136</sup> is not always feasible or possible to follow (e.g. in winter). Vitamin D can also be obtained from dietary sources such as fatty fish and egg yolk for omnivores and mushrooms for vegetarians and vegans. Children with decreased dietary intake, lack of sun exposure or with a dark skin are at risk of a hypovitaminosis D and are encouraged to supplement with 600 IU of vitamin D3. The abstinence of milk and milk products in a vegan diet decreases the intake of **calcium**; this is relevant for infants after being weaned from breast milk or infant formulas. Vegetables low in oxalate such as broccoli, Chinese cabbage or collards are good sources of bioavailable calcium. Alternatively, calcium-fortified plant drinks, juices and calcium-rich mineral water are available. The FCN recommends a supplementation with 400 IU/day for every infant up to 1 year, regardless the type of nutrition and

with 600 IU/D for toddlers up to 18 years<sup>122</sup>. If this recommendation is followed, the risk of rickets or hypocalcemia is very low.

As with other micronutrients, the content of **iodine** in breast milk is dependent on the nutritional status of the mother<sup>139</sup>. The recommended intake in breastfeeding mothers is discussed in chapter 7.1. As seen in chapter 6.2 iodine is a critical micronutrient in an unsupplemented vegan diet. Low intakes during pregnancy and breastfeeding can exacerbate an iodine deficiency, in both mother and infant. Infants fed with formula milk receive the recommended daily supply of 80 µg per day. A risk of iodine deficiency can occur if they are solely fed with self-prepared food. To prevent a deficiency the FCN-publication “Ernährung in den ersten 1000 Lebenstagen” recommends partially replacing self-prepared food with iodine supplemented food or adding iodine supplementation of 50 µg per day<sup>124,140</sup>.

As mentioned in chapter 6, an unsupplemented vegan diet is lacking in **vitamin B<sub>12</sub>**. A prolonged vitamin B<sub>12</sub> deficiency will lead to a severe and potentially not fully reversible delay in the neuropsychological development of affected children. Vitamin B<sub>12</sub> deficiency under a vegetarian diet (measured by MMA and holoTCII) has been reported for pregnant women (62%) and for children (25% - 86%)<sup>99</sup>. Breastfed infants will suffer from birth their mother's milk is low in vitamin B<sub>12</sub>, this is the reason we recommend to test the vitamin B<sub>12</sub> status of the lactating mother. There are so far no studies we know giving evidence on the necessary quantity and time interval of orally supplied vitamin B<sub>12</sub> to reach a physiologically adequate intracellular concentration, as shown by a normalized measurement of MMA. The recommended intake of vitamin B<sub>12</sub> for breastfed vegan infants is 0.4 µg/day during the first 4 month of life and 0.8 µg/day, beginning at 5 months of age and should be increased up the recommended intake of 3.0 µg/day for adolescents<sup>52</sup>. Because absorption of vitamin B<sub>12</sub> is dose dependent saturated, a supplementation could be as followed (table 7-2)<sup>141</sup>.

**Table 7-2 Recommended dietary supplement values for preserving normal B12 levels in persons becoming vegetarians<sup>141</sup>.**

Age	LARN <sup>a</sup> (PRI) <sup>c</sup> (µg/day)	EFSA <sup>b</sup> (AI) <sup>d</sup> (µg/day)	Daily multi-dose	Daily single-dose (µg/day)
<b>6-12 months</b>	0.7	1.5	1 µg x 2	5
<b>1-3 years</b>	0.9	1.5	1 µg x 2	5
<b>4-6 years</b>	1.1	1.5	2 µg x 2	25
<b>7-10 years</b>	1.6	2.5	2 µg x 2	25
<b>11-14 years</b>	2.2	3.5	2 µg x 3	50
<b>16-64 years</b>	2.4	4.0	2 µg x 3	50
<b>65+ years</b>	2.4	4.0	2 µg x 3	50
<b>Pregnancy 2.6</b>	2.6	4.5	2 µg x 3	50
<b>Breastfeeding 2.8</b>	2.8	5.0	2 µg x 3	50

<sup>a</sup> LARN is an Italian acronym meaning Reference Levels of Nutrient and Energy Intake for the Italian Population.

<sup>b</sup> European Food Safety Authority.

<sup>c</sup> Population reference intake.

<sup>d</sup> Adequate intake.

Different health associations state that well-balanced and planned vegetarian and vegan diets are compatible with a healthy upbringing and are appropriate at all stages of fetal, infant, child and adolescent growth<sup>6,142</sup>. The focus on well-balanced and planned diets needs to be emphasized in all recommendations, including the elements listed in **table 7-3**.



**Table 7-3: Recommendations for children fed a vegan diet resp. with a vegan mother (adapted from<sup>143</sup>)**

Infants (1-12 months)	Toddlers (Td, 2-4 years) and children (> 4 years)
<p>Breast fed: if the mother is on a vegan/vegetarian diet, a vitamin B12 analysis (and supplementation if necessary) is recommended</p> <p>Formula-fed: adapted soy-infant formula</p> <p>Complementary food:</p> <ul style="list-style-type: none"> <li>Breast milk (BM) or infant formula until 12 months</li> <li>Pulses (puréed) / tofu is possible from 6 months onwards</li> <li>Energy-dense solid food, containing with ALA-rich oil supplements (linseed, walnut or rapeseed)</li> <li>Consider an iron supplement (mainly in BM fed infants after 6 months)</li> <li>Vitamin K, as all infants (using <i>Quick</i> as a lab marker)</li> <li>Vitamin D supplement</li> <li>Supplement Vitamin B<sub>12</sub></li> <li>evaluate zinc and iodine intake</li> <li>Dietitian/pediatrician support (diet diary / lab controls)</li> </ul>	<p>Check and ensure</p> <ul style="list-style-type: none"> <li>Caloric intake (percentiles)</li> <li>Limit raw food in Td (lower digestibility, difficult to ingest, caloric density)</li> <li>Advise grinding nuts (choking in Td)</li> <li>Calcium intake (Ca-suppl. drinks)</li> <li>Iodine supplementation (salt)</li> <li>Vitamin B<sub>12</sub> supplementation</li> <li>Vitamin D according to serum level</li> <li>Dietitian/pediatrician support (based on the analysis of 3-day dietary records / lab controls)</li> </ul>
<p><b>Adolescents: As above, additionally enquire about motivation / underlying eating disorders</b></p>	

### Amendment to the 2006 report

There is still a lack of data whether the basic nutritional requirements are met and whether the development of children and adolescents fed on a vegan diet is secured on a long-term perspective. These data should be collected and analyzed more systematically. There is in our view up to now no evidence that a vegan diet can be recommended for these age groups. However, parents and/or caretakers desiring to have their children and adolescents follow a vegan diet should follow at least the recommendations listed above.

## 7.3 Ageing

**Lead authors: Roger Darioli, Beatrice Baumer**

No longitudinal prospective study was found monitoring very long-term vegan diets (including the assessment of specific dietary patterns and degree of adherence) and their impact on health. The consequences of long-term adherence to a vegan diet compared to the impact of a dietary switch to a vegan diet at a later stage of life have also not been investigated.

No specific vegan dietary recommendations have been made for an ageing population<sup>144,145</sup>.

General nutrient recommendations for older adults are often higher than for healthy adults (<65 years old), some of the concerned nutrients are those, which are often at risk of deficiency in a vegan diet: protein, vitamin D, zinc, vitamin B<sub>12</sub> and calcium. A vegan diet could therefore exacerbate nutritional deficiencies, which could be critical in the case of polymorbidity and frailty<sup>145</sup>. In particular, protein recommendations for older adults following a vegan diet should be investigated, taking into account the higher needs at older ages (1.0-1.2 g/kg body weight) and the possible lower digestibility of plant proteins.

A matched cross-sectional study with institutionalized older adults, with 22 female and 7 male vegetarian (females: 84.1 ±5.1yrs, males: 80.5 ±7.5 yrs) and 23 female and 7 male bon-vegetarians (females: 84.3

$\pm 5.0$  yrs, males:  $80.6 \pm 7.3$  yrs) concluded that a vegetarian diet does not have a negative impact on the nutritional status and health indicators (blood profile, anthropometrics, handgrip strength)<sup>146</sup>.

A Taiwanese longitudinal study has several limitations, the main being the short duration of the longitudinal study (1 year), the other being the unknown number of older vegans in the cross-sectional part of the study. The metabolic profile of participants following a plant-based diet (vegan, lacto-vegetarian, ovo-lacto-vegetarian) analysed in this study seems to be more favourable than that of omnivores in all age groups<sup>147</sup>.

Age itself is a risk factor for most non-communicable diseases, and this will be discussed in chapter 8.

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### Amendment to the 2006 report

The previous report emphasized the importance of a micronutrient supplementation, which can be confirmed, based on the data of chapter 6.

No mention was made for protein requirements. Newer data recommend a higher protein intake for older adults. Covering this intake with a vegan diet could be problematic, as seen for all age groups, in chapter 6. Therefore, specific dietary guidelines could be helpful.

The impact of a long-term vegan diet is still a field to be investigated for older adults, taking into account both risk and beneficial factors. In particular, the impact of a long-term nutrient deficiency (as suggested in chapter 6) could increase the vulnerability of older vegans.

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## 8 Vegan diets and non-communicable diseases

In this chapter, the focus is on the impact of vegan diets on health, with the aim to assess whether a vegan diet is associated with an increased or decreased risk for major non-communicable diseases, such as overweight/obesity, type 2 diabetes, cardiovascular diseases (CVD) and some cancer forms and other diseases. In the following chapters, the main results of recently published scientific studies are presented, based on vegan data, but including data on vegetarian diets, when these are compared to vegan diets. The evaluation of scientific evidence of the results was based on a grading system developed by the American Diabetes Association (ADA) to clarify and codify the evidence that forms the basis for the recommendations to improve health outcomes<sup>12</sup>.

### 8.1 Overweight / obesity

**Lead author: Roger Darioli**

#### 8.1.1 Prevention

Observational and case-control studies show that a long-term vegan diet is associated with a lower body weight than an omnivorous diet<sup>148-150</sup>, no causality can be deducted from such studies. A follow-up study (EPIC-Oxford) over 5.3 years shows that a vegan diet does not prevent age-associated weight gain, however, the annual weight gain is significantly lower in the vegan participants (males +284 g, females +303 g), compared to omnivores (males: +406 g, females +423 g). The mean age-adjusted BMI ( $\text{kg/m}^2$ ) increased from values of 22.6 to 23.2 (male vegans) and from 22.4 to 22.9 (female vegans), whereas omnivores had an initial mean age-adjusted BMI of 24.7 (males) and 23.8 (females), and increased to 25.3 and 24.8 respectively<sup>151</sup> (**figure 8-1**). In this study the vegan group had a lower mean energy intake (-279 kcal/day, compared to omnivores).

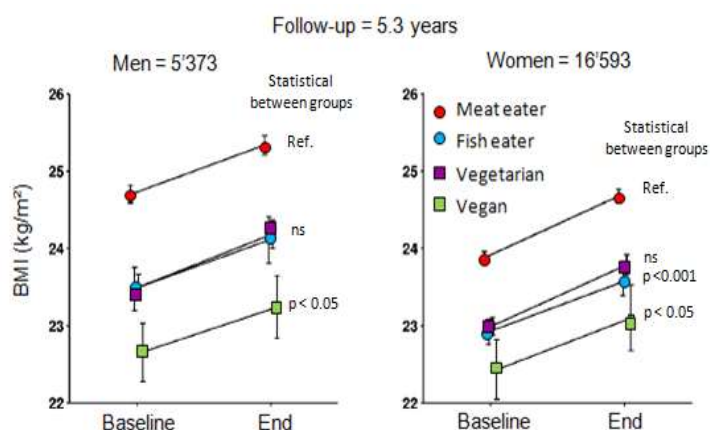


Figure 8-1: Age-adjusted mean body mass index (BMI) at baseline and follow-up by diet groups for men and women who were in the same diet group at both times<sup>151</sup>.

### 8.1.2 Weight loss in overweight / obese subjects

The question thus arises, whether a vegan diet could be an effective weight loss strategy in overweight or obese subjects. Several systematic reviews and meta-analysis of mostly randomized controlled trials (RCT), in particular those of Huang et al.<sup>152</sup>, who selected studies according to Jadad et al. quality criteria<sup>153</sup> and those of Barnard et al.<sup>154</sup> have shown that a vegan diet can lead to significantly greater weight loss in comparison to their control (non-vegetarian) diet groups (**figure 8-2**).

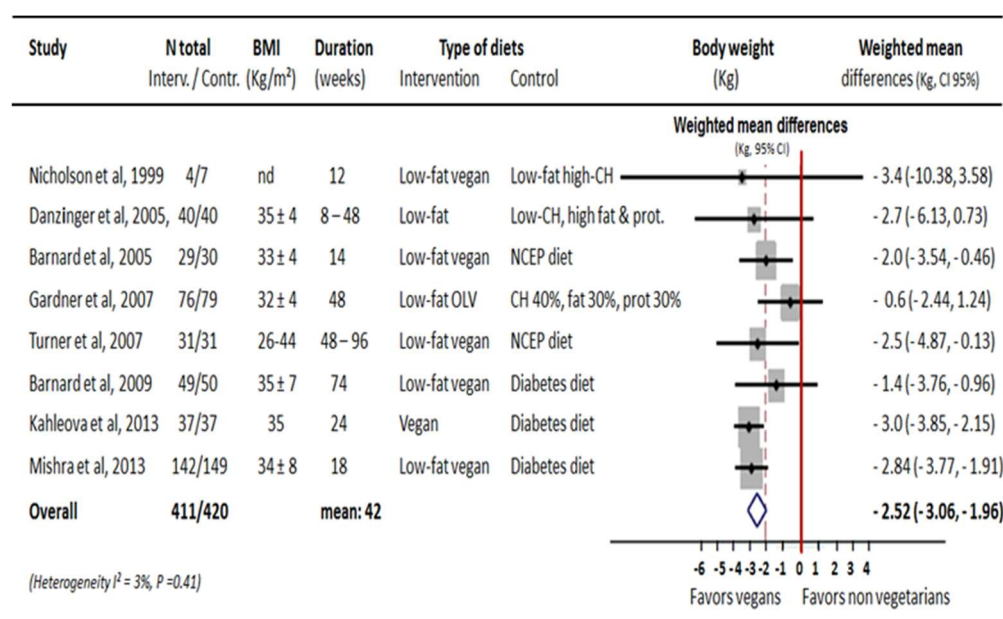


Figure 8-2: Pooled weighted mean differences in weight reduction observed intervention trials for vegan diets as compared to non-vegetarian diets<sup>152</sup>

However, these changes are not statistically different from other weight-loss diets reported in the recent systematic review and meta-analysis from Tobias et al.<sup>155</sup>. Studies included in this systematic review included energy-reduced omnivore diets, ovo-lacto-vegetarian diets, or Atkins diets<sup>156</sup>.

Most of these studies have a high heterogeneity and are of a rather short duration in addition to other limitations that reduce their scientific evidence to the level C, based on the grading system developed by the American Diabetic Association<sup>12</sup>. Therefore, long-term intervention trials are needed to investigate the effects of vegan and vegetarian diets, the caloric restriction on weight control and the cardiometabolic risk.

In conclusion, the data shows that there is no evidence that a vegan diet has a definite superiority in comparison to a balanced diet for weight control or to weight loss diets recommended for overweight or obesity.

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### Amendment to the 2006 report

This review based on observational studies and randomized controlled trials confirm previous observations of the previous report, showing that vegan and vegetarian diets are associated with lower body weight than non-vegetarian diets. But, in addition to the previous report, recent data indicate that:

- a vegan diet does not prevent an age-associated weight gain,
  - however the yearly weight gain was significantly lower in the vegan participants, compared to e.g. omnivores among the participants to the follow-up study (EPIC-Oxford)
  - according to the systematic reviews and meta-analyses on interventional trials (RCT), vegan diets induce a light reduction of body weight compared to the non-vegetarian diets. However, there is no evidence that vegan diets have a definite superiority compared to a balanced diet for weight control or to weight loss diets recommended for overweight or obesity.
- 

## 8.2 Type 2 diabetes

**Lead author: Roger Darioli**

The role of nutrition and other life-style factors in the prevention and treatment of type 2 diabetes (T2DM) has been recognised. There is good evidence (grade A) of the impact of a balanced energy intake and weight loss (-5% of body weight), as well as B-grade evidence for diets with fruit and pulses as the main carbohydrate sources that are rich in fibres<sup>157</sup>. These are elements of a well-planned vegan diet. Therefore, recent epidemiological literature was screened in order to evaluate the impact of a self-chosen vegan diet on the risk of T2DM (preventive effects) and the efficacy of a vegan diet as a nutritional therapeutic approach.

### 8.2.1 Prevention

A case-control study was performed by Tonstad et al.<sup>158</sup> with the Adventist Health Study-2 (SDA) cohort, with 60'903 participants. The data were corrected for 10 factors, including age, sex, physical activity and BMI. The ensuing results showed that the odds ratio (OR) for the prevalence of self-declared T2DM was 0.51 for vegans (CI 0.40 - 0.66), 0.54 for ovo-lacto-vegetarians (CI 0.49 - 0.60), 0.70 for pesco-vegetarians (CI 0.61 - 0.80), and 0.76 for semi-vegetarians (CI 0.40 - 0.66), when compared to the reference group (omnivores). Furthermore, in a subgroup of 42'017 participants in this SDA cohort, the same authors reported after a follow-up of two years, a lower incidence of T2DM for vegans (0.54%), for ovo-lacto-vegetarians (1.08%), for pesco-vegetarians (1.29%), and semi-vegetarians (0.92%), when compared to the omnivores (2.12%,  $p < 0.001$ )<sup>159</sup>. However, as indicated by the authors, a number of study limitations must be considered when interpreting these findings.

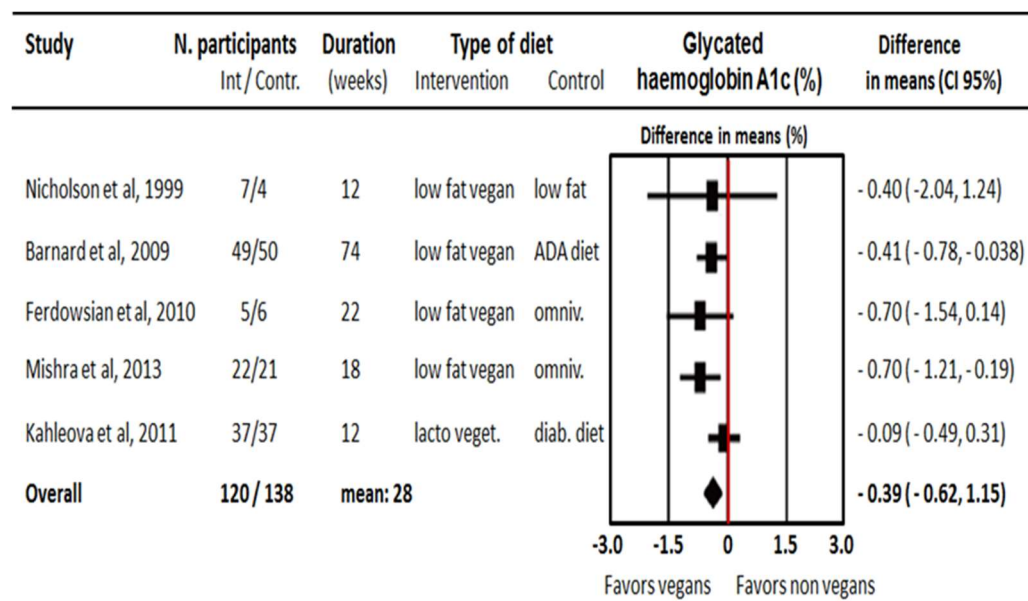
Two cross-sectional studies, performed in Asian countries<sup>160,161</sup> have contradictory results; these studies were therefore not further taken into account in this review, due to the different dietary and lifestyle patterns.

A direct comparison with other lifestyle and dietary choices, which have shown a protective effect (e.g. Mediterranean diet<sup>162-164</sup>) is still lacking, therefore vegan diets are not specifically recommended to delay T2DM<sup>165</sup>.

### 8.2.2 Therapy

For their systematic review, Yokoyama et al.<sup>166</sup> found only 6 intervention studies fulfilling the criteria established by the "Cochrane Handbook for Systematic Reviews Intervention"<sup>11</sup> among the 477 studies published between 1947 and 2013. Vegan diets (N=4) and lacto-vegetarian (N=1) were compared to control diets, using the glycated hemoglobin A1c (HbA1c) measurements as the outcome (**figure 8-3**). Of the 5 studies with 258 diabetic participants included for 12 to 74 weeks (mean = 28 weeks), three were randomized, two

were non-randomized comparisons, and one was a cluster randomized trial. In the pooled analysis, consumption of vegan diets was associated with a significant mean reduction in HbA1c (-0.39% 95% CI: -0.62 to -0.15;  $P=0.001$ ;  $I^2 = 3.0$ ;  $P$  for heterogeneity = 0.389), compared to non-vegetarian diets.



**Figure 8-3: Pooled mean changes in glycated hemoglobin A1c level in response to the vegan and vegetarian diet as compared to other control diets in type 2 diabetes** <sup>166</sup>

The corresponding mean reduction in fasting blood glucose levels was not significant (-0.36 mmol/l; 95% CI: -1.04 to 0.32;  $P = 0.301$ ;  $I^2 = 0$ ;  $P$  for heterogeneity = 0.710). In this analysis, consumption of vegetarian diets was associated with significant mean differences in energy intake (-139.8 kcal; 95% CI: -232.8 to -46.7;  $P = 0.003$ ) as well as for the other macronutrients<sup>166</sup>. The magnitude of the effect size is approximately one-half of that seen with metformin, which is used as first-line oral therapy for elevated HbA1c levels<sup>167</sup>.

A further systematic review on the same topic was conducted by Ajala et al.<sup>168</sup> providing a succinct but robust evidence base to guide clinicians and patients on the most suitable dietary intervention to improve glycemic control. 16 RCTs were included ( $n = 3'073$  in the final analysis across 3'460 randomly assigned individuals). Compared with their respective control diets, a greater improvement in HbA1c reductions was observed for Mediterranean diet (-0.47%,  $p < 0.00001$ ,  $I^2 = 82\%$ ,  $N = 3$ ) than for low carbohydrate (-0.12%,  $P = 0.04$ ,  $I^2 = 75\%$ ,  $N = 8$ ), for low-glycemic index (-0.14%  $P = 0.008$ ,  $I^2 = 80\%$ ,  $N = 3$ ) or high-protein diets (-0.28%,  $P < 0.00001$ ,  $I^2 = 60\%$ ,  $N = 2$ ). Low-carbohydrate and Mediterranean diets led to greater weight loss (-0.69 kg,  $P = 0.21$ , and -1.84 kg,  $P < 0.00001$ , respectively).

For the only vegan RCT reported in the Ajala review (by Barnard et al.)<sup>168</sup>, a significant reduction in HbA1c was achieved in comparison to the diabetic diet recommended by the American Diabetic Association, when the effects were assessed before the medication changes (-0.41%,  $P = 0.03$ ). The changes were however non-significant (-0.20%,  $P = 0.43$ ) when reported for the intention-to-treat analysis.

According to the review of the existing literature, Ajala et al.<sup>168</sup> therefore consider that low-carbohydrate, low-glycemic index, Mediterranean, and high protein diets are effective in improving glycemic control and should be therefore considered in the overall strategy of T2DM management, but no specific recommendations are given for the vegan/vegetarian diets<sup>157,169</sup>.

Finally, Emadian et al.<sup>170</sup> conducted a recent systematic review of eleven RCTs, including the only vegan trial from Barnard et al.<sup>171</sup> in order to assess the effects of various dietary interventions on glycemic control in overweight and obese adults with T2DM, when adjusted for weight loss. Overall, they conclude, "*there is currently insufficient evidence to suggest that any particular diet is superior in treating overweight and obese*

*patients with T2DM* “. However, although the Mediterranean, vegan and low-GI diets appear to be promising, these authors consider that “*further research that controls for weight loss and the effects of diabetes medications in larger samples is needed* “.

In conclusion, given the limited number of studies with sufficient methodological quality providing a low level of scientific evidence (C), new findings are required to assert that vegan diets offer more advantages than non-VGT for the metabolic control of type 2 diabetes.

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### Amendment to the 2006 report

No mention was given in the previous report on vegan/vegetarian diets and diabetes.

For the prevention of T2DM, the Adventist Health Study-2 cohort observational studies suggest that vegan diets are associated with a lower prevalence and incidence of diabetes in comparison to the other diets.

Before specifically recommending vegan diets, further research is required for a direct comparison with other lifestyle and dietary choices, which have also been shown to be protective (e.g. Mediterranean diet).

For the metabolic control of T2DM, current knowledge is based on a small number of interventional studies (RCT) with small numbers of participants and mostly of short duration. Overall, the data indicate that vegan diets may result in a mild decrease in HbA1c compared to the control diets. However, the magnitude of this effect is comparable to that observed with the recommended diabetic diets.

## 8.3 Cardiovascular diseases

### Lead author: Roger Darioli

Today, cardiovascular diseases (CVD), such as ischemic heart disease (IHD) and stroke significantly increase the burden of disease in Switzerland. They cause premature deaths and CVD morbidity contributes to the rising costs in the health sector. In 2014, CVD were the first cause of mortality as well in women (34%) as in men (31%). Among CVD deaths, 78% were due to cardiac origin, namely IHD and myocardial infarction, and 16.5 % to strokes. Therefore CVD have been included in National Strategy for the Prevention of Non-communicable diseases 2017–2024»<sup>172-174</sup>.

### Risk factors for cardiovascular diseases

Dietary habits influence the CVD risk, either by effecting risk factors such as blood pressure, cholesterol, body weight and diabetes, or through other effects. Healthy dietary practices have been recommended as a cornerstone of CVD prevention in all individuals for decades<sup>175,176</sup>. In the last decade, plant-based dietary patterns have become a popular recommendation, due to a variety of reported health benefits to overall health and to cardiovascular (CV) risk and disease in particular<sup>177-179</sup>. However, most evidence on the relation between nutrition and CVD is based on observational studies; randomized clinical trials estimating the impact of diet on clinical endpoints are scarce. The aim of this chapter is to highlight scientific knowledge concerning the influence of vegan diets on CV risk factors and CVD morbidity and mortality, namely ischemic heart disease (IHD) and cerebrovascular disease (CeVD).

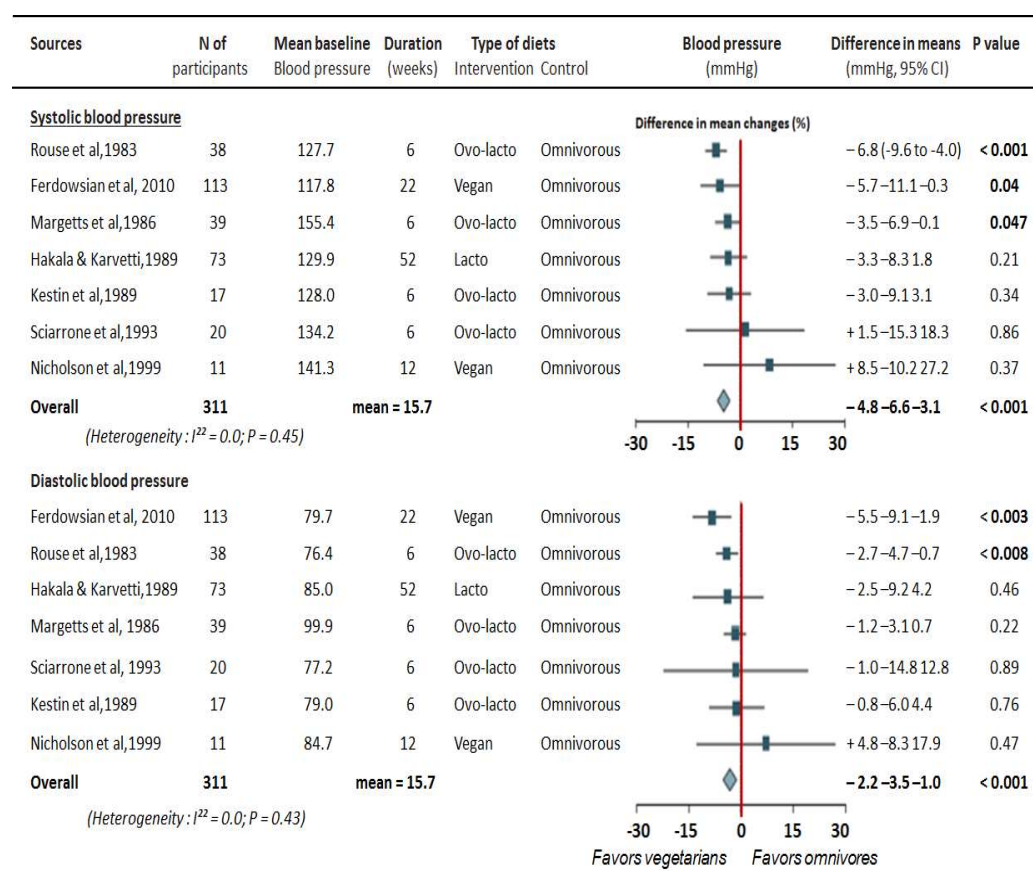
### 8.3.1 Hypertension

The main diet-related determinants of hypertension are high salt intake, obesity and excess alcohol consumption. Western vegetarians have a lower average BMI than non-vegetarians, but do not necessarily have low intakes of salt and alcohol<sup>180</sup>. To examine the association between vegan and vegetarian diets and blood pressure, Yokoyama et al. conducted a systematic review and meta-analysis<sup>181</sup>. Of the 258 studies identified, 32 observational studies and 7 clinical controlled trials met the inclusion criteria. In the 32 observational cross-sectional studies (total n=21'604 participants; mean age 46.6 years), consumption of vegetarian diets was also associated with both a significantly lower mean systolic BP (–6.9 mmHg; 95% CI:



-9.1 to -4.7;  $P < 0.001$ ,  $I^2 = 91.4$   $P < 0.001$  for heterogeneity) and with a lower diastolic BP (-4.7 mmHg; 95% CI: -6.3 to -3.1;  $P < 0.001$ ,  $I^2 = 92.6$   $P < 0.001$  for heterogeneity) compared with the consumption of omnivorous diets. A significant reduction of systolic BP (-28 to -4.9 mmHg) was also observed in the four vegan studies. However, due to the wide heterogeneity of these results and the multiple limitations of such studies, the scientific evidence for the anti-hypertensive effects of vegan and vegetarian diets must be considered as low (C).

Yokoyama et al. also performed a meta-analysis of the seven clinical controlled trials, with 311 participants (mean age 44.5 years), mainly without hypertension see **figure 8-4**<sup>181</sup>. The consumption of vegetarian (N= 5) or vegan (N= 2) diets was associated with a significant reduction in mean systolic BP (-4.8 mm Hg; 95% CI: -6.6 to -3.1;  $P < 0.001$ ,  $I^2 = 0$ ,  $P = 0.45$ ) and diastolic BP (-2.2 mmHg; 95% CI: -3.5 to -1.0;  $P < 0.001$ ,  $I^2 = 0$ ,  $P = 0.43$ ), compared to omnivorous diets. The magnitude of the anti-hypertensive effect was less pronounced here than in the observational studies. Moreover, the changes in systolic and diastolic BP were significant only in the oldest of five vegetarian trials.



**Figure 8-4: Pooled systolic and diastolic blood pressure responses to vegan and vegetarian diets in clinical trials<sup>181</sup>**

However, diverging results were observed between the two vegan trials (**figure 8-4**). Due to several significant limitations of these controlled trials such as small sample size, short duration and lack of adjustment for confounding factors, only C-grade of evidence can be attributed to this meta-analysis. As concluded by these authors, “*despite consumption of vegetarian diets is associated with lower BP, further studies are required to clarify which types of vegetarian diets are most strongly associated with lower BP*”. Overall, these effect sizes are similar to those observed with commonly recommended lifestyle modifications, such as adoption of a low-sodium diet or a weight reduction of 5 kg, and are approximately half the magnitude of those observed with pharmaceutical therapy, such as administration of angiotensin-converting enzyme inhibitors to individuals with hypertension<sup>182,183</sup>.

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## Amendment to the 2006 report

New observational studies confirm the association between the vegetarian diets and the reduction of BP in comparison with non-vegetarian diets, as presented in the previous report. Recent RCTs have shown that vegetarian diets can contribute to a possible significant reduction of systolic and BP as compared with omnivorous diets, but conflicting results were observed with vegan diets.

Although there seems to be an association between vegetarian diets and a lower BP, further studies are required to clarify the impact of vegan diets on BP.

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### 8.3.2 Dyslipidemia

Theoretically, in comparison with omnivorous diets, vegan and vegetarian diets may have a beneficial effect on the blood lipid profile, due to the lower intake of saturated fats as well as the high fibre intake (see **table 6-1**).

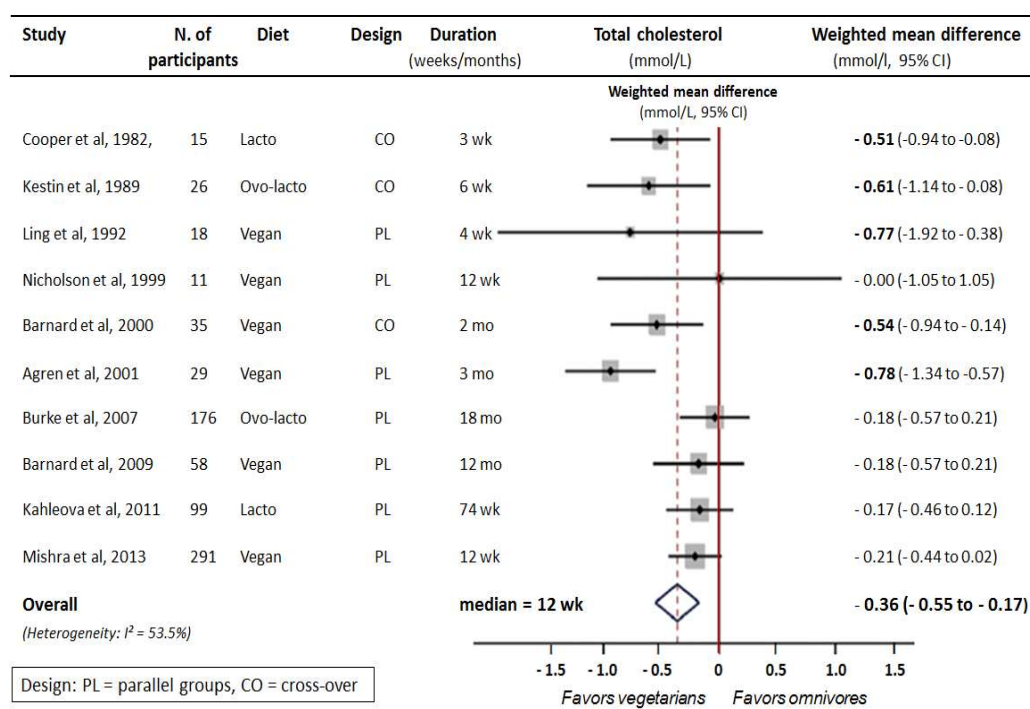
Several cross-sectional studies have shown that concentrations of TC, LDL-C, and TG were lower in vegetarians than in omnivores<sup>184-186</sup>.

A recent systematic review and meta-analysis of the published RCTs was conducted by Wang et al.<sup>187</sup> to comprehensively assess the overall effects of vegetarian diets on blood lipids. Among these 10 studies, 6 included a vegan diet, 2 included a ovo-lacto-vegetarian diet, and 2 included a lacto-vegetarian diet, with a total of 774 participants treated by the diet during 3 weeks to 18 months (median = 12 weeks). In these trials, a majority of recruited patients were diabetics or with BMI > 25 kg/m<sup>2</sup> and some were receiving lipid-lowering agents. The results provide evidence that vegetarian diets significantly lower the mean blood concentrations of total cholesterol, LDL-cholesterol and HDL-cholesterol (pooled estimated changes were -0.36 mmol/l,  $P < 0.001$ , -0.34 mmol/l,  $P < 0.001$ , and -0.10 mmol/l,  $P < 0.001$  respectively), without affecting triglyceride levels. Moderate to high heterogeneity of the results was detected for total cholesterol ( $I^2 = 53.5\%$ ) and LDL-cholesterol ( $I^2 = 72.4\%$ ).

As shown in **figure 8-5**, the observed reduction in cholesterol levels was significant in 2 of 4 vegetarian diet studies. Among the 6 vegan studies, the estimated changes in cholesterol ranged from -0.78 to 0 mmol/l, and were significant only in two older studies: -0.54 mmol/l, CI 95%: -0.94 to -0.14 and -0.78 mmol/l, CI 95%: -1.34, to -0.57<sup>187</sup>.

Again, the studies included in this meta-analysis suffer from several limitations acknowledged by the authors and consequently reduce the level of the scientific evidence (C). Moreover, the evidence that these changes in lipid profile induced vegetarian diets preventing CVD is still lacking. By comparison, available evidence exists for the dietary patterns such as the Mediterranean diet, which has been more extensively evaluated and has been proven to be effective to reduce CV risk factors, as well as to contributing to CVD prevention<sup>188,189</sup>.





**Figure 8-5 Effects of vegetarian diets on total cholesterol concentrations as compared to omnivorous diets in interventional trials<sup>187</sup>.**

## Amendment to the 2006 report

Recent interventional studies have shown that vegan and in general, vegetarian diets possibly lead to a mild reduction of total cholesterol and LDL-cholesterol, when compared to omnivorous diets. This reduction is less pronounced than the one indicated in the previous report. Moreover, evidence for the claim that these changes of the lipid profile have a protective effect on CVD is still lacking.

### 8.3.3 Cardiovascular diseases

A collaborative analysis of five prospective studies, by Key and al., is frequently reported in the literature<sup>190</sup>. This study showed that mortality from IHD was 26% lower in vegans (RR 0.74, 95% CI: 0.46 - 1.21), 34% than for vegetarians (RR 0.66, CI: 0.52 - 0.83, significant), both when compared to omnivores. These older results were based on observational studies that suffered from key limitations. More solid evidence is necessary before making recommendations for the general population. Therefore, the following chapter aims to summarize the scientific literature established up to the end of January 2018 in order to confirm the possible contribution of vegan or vegetarian diets to reduce the risk of CVD, including IHD and strokes.

#### 8.3.3.1 Prevention of cardiovascular diseases

To examine whether vegan and vegetarian diets, as compared to non-vegetarian diets, are associated with reduced incidence of a first CV event, Crowe et al.<sup>191</sup> have analyzed the risk of hospitalization following the incidence of non-fatal or fatal IHD events among 44'561 men and women involved in the EPIC–Oxford study. After an average follow-up of 11.6 years, vegetarians (including vegans) had a 32% lower risk (95% CI: 0.58 - 0.81) of IHD events than did non-vegetarians, when adjusted for age, smoking, alcohol, physical activity, educational level, and Townsend Deprivation Index and use of oral contraceptives or hormone therapy for menopause in women. This rate was only slightly attenuated, but remained significant, after additional adjustment of BMI. When this analysis was stratified by sex a significant risk reduction of IHD events of -26% (95% CI: 0.58 - 0.95) in both men and women (-36%; 95% CI: 0.51 - 0.81) was observed.

No specific analysis was performed here to examine whether vegan diets might be associated with similar benefits for CerVD or CVD in general.

The data reported by Christiansen *al.*<sup>192</sup> issue from a cohort comprising 6'532 members of the Danish Seventh-day Adventist Church (SDA) and another cohort totalizing 3'720 Baptists followed in the Danish National Patient Register from 1977 to 2009. The SDA advocates against alcohol consumption and tobacco smoking and recommends an ovo-lacto-vegetarian diet, but not specifically a vegan diet. In addition, members of SDA were expected to be physically active and have stable social relationships. Members of the Baptist community were encouraged not to smoke or drink alcohol.

During the 12-year follow-up, compared with the general Danish population, the SDA members experienced a standardized incidence ratio of a first IHD that was significantly lower in women (-9%; 95% CI: 0.83 - 0.99), but not in men (-8%; 95% CI: 0.83 - 1.03). For a first CerVD this ratio was not significantly lower neither in women (-3%; 95% CI: 0.88 - 1.08) nor in men (-7%; 95% CI: 0.81 - 1.06).

Similar trends were obtained among the Baptists, with a significant lower incidence ratio of IHD in women (-22%; 95% CI: 0.69 - 0.89) but not in men (-3%; 95% CI: 0.86-1.10), while the ratio for CerVD was not significantly reduced, either in women (-6%; 95% CI: 0.82 - 1.07) or in men (-8%; 95% CI: 0.79 - 1.08). Whether similar results could be obtained by vegan diets needs to be determined. Concerning the key limitations of this observational study, namely the lack of adjustment for confounding factors, caution is needed when interpreting these results.

In summary, according to the very small number of studies available to date (two Danish studies, one EPIC-Oxford), and to the limitations of such observational studies, the scientific evidence in favour of vegetarian diets for the primary prevention of CVD is low (level C of evidence). Nevertheless, the results reported here show that vegetarian diets are associated with a significant reduction in the risk of hospitalization for a first IHD in women, but not clearly in men, and with a non-significant reduction for CerVD. Whether vegan diets may have similar effects has not yet been demonstrated. Further research is clearly required to prove the potential benefits of vegan and vegetarian diets for the primary prevention of CVD.

### 8.3.3.2 Cardiovascular diseases mortality

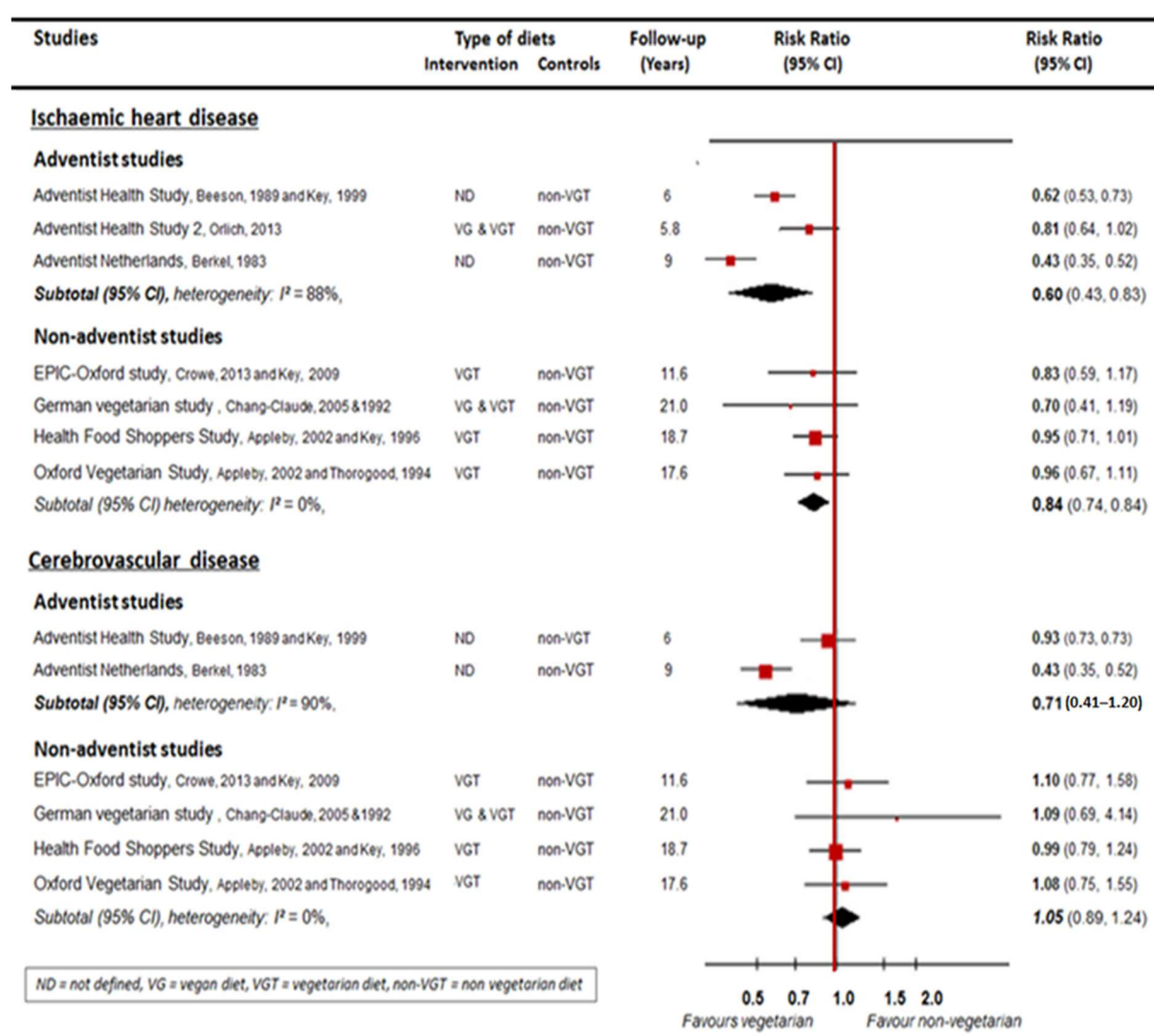
The review of scientific literature published between 2007 and January 2018 identified three systematic reviews of relevant prospective cohort studies evaluating the link between the vegetarian diets and the risk of CV mortality<sup>193-195</sup>.

The first systematic review and meta-analysis of Huang *et al.*<sup>193</sup> incorporated seven prospective cohort studies of which three were already included in the series of Key *et al.*<sup>190</sup> published in 1999. Among a total of 124'706 participants recruited between 1955 and 1999 and followed during 10 to 23 years, the IHD mortality was significantly lower (-29%; 95% CI: 0.56 - 0.87;  $I^2 = 31\%$ ) in vegetarians and vegans than in non-vegetarians. However, this association was neither significant for CerVD mortality (-12%, 95% CI: 0.70 - 1.06;  $I^2 = 31\%$ ), nor for circulatory diseases mortality (-16%, 95% CI: 0.54 - 1.14;  $I^2 = 58\%$ ).

Kwok *et al.*<sup>194</sup> carried out the second systematic review and meta-analysis of eight prospective cohort studies. Among them, the cohort of Adventist Health Study-2 was added to the 7 cohorts included by Huang *et al.*<sup>193</sup>, but with different sample sizes and follow-ups. Their objectives were firstly to update the current understanding of the lower risk of CV mortality associated with vegetarian diets (pesco-, semi-, ovo-lacto and vegans) compared to non-vegetarian diets. A second objective was to determine whether the positive findings could be specific to the vegetarian diets alone or to the healthier lifestyles observed among the members of the cohort of the Seventh Day Adventists Church, by comparison to other cohort studies. Seven cohort studies were included in this pooled analysis to obtain a level of quality deemed to be moderate in five studies and low to moderate in 2 studies. In addition to the lack of collected data, there were also differences in the use of adjustments for confounders such as weight, smoking and alcohol in vegetarian studies.

As illustrated in **figure 8-6**, the authors found that 3 SDA studies showed a significant mean reduction of IHD mortality (-40%; 95% CI: 0.43 - 0.80). The non-SDA studies confirm this risk reduction, but to a lesser extent (-16 % for the pooled results; 95% CI 0.74 - 0.96,  $I^2 = 0\%$ ,  $P = 0.92$ ). When combining the SDA and non-SDA groups, the risk reduction was -29% (95% CI: 0.57 - 0.87;  $I^2 = 83\%$ ). This risk reduction associated with vegetarian diets was significant in men (-19%; 95% CI: 0.68 - 0.97) and near to the statistical significance in women (-26%; 95% CI: 0.54 - 1.01), with a large heterogeneity ( $I^2 = 88\%$ ,  $P = 0.0002$ ) of the results, as compared to with the mean of the 4 non-SDA studies: (-16 %; 95% CI 0.74 - 0.96,  $I^2 = 0\%$ ,  $P = 0.92$ ).

For CerVD mortality, the risk reduction pooled for the two SDA studies was 29% (95% CI 0.41 - 1.20;  $I^2 = 83\%$ ), but again with a high heterogeneity of these results. In contrast, no significant differences were found in any of the four non-SDA studies, nor in the mean risk of CerVD (+5%; 95% CI: 0.89 - 1.24). However, when SDA and non-SDA studies were pooled, there was a small and non-significant reduction in relative risk (-7%; 95% CI: 0.70 - 1.23;  $I^2 = 79\%$ ). In this meta-analysis, no data were provided for overall CV mortality.



**Figure 8-6: Meta-analysis of vegetarian diets and risk of death by ischaemic heart disease and cerebrovascular disease cohorts as compared to non-vegetarian diets, stratified by Seventh-Day Adventist and non-Adventist cohorts<sup>194</sup>.**

Overall, these data supporting the benefits of vegetarian diets are derived mainly from SDA studies that have different lifestyles and other factors that are not generalizable to the wider population. A similar point

of view is given by Kwok et al.<sup>194</sup>, which concludes that “the reduction in IHD and all-cause mortality with vegetarian diet stems mainly from the Adventist studies, and there is much less convincing evidence from studies conducted in other populations. Once the SDA studies have been excluded, the results are either less significant or with a lesser magnitude of benefit, and this raises the concern that the non-dietary factors (confounders) in SDA lifestyle may be responsible for the risk reduction among the vegetarian studies. In addition, among men there appears to be greater benefit of vegetarian diet compared to women. In view of these inconsistent findings, we conclude that the benefits of vegetarian diet for reducing death and vascular events remain unproven.”

A third recent systematic review with meta-analysis performed by Dinu et al.<sup>195</sup> included a pool of three SDA and four non-SDA cohort studies, among them six were already analysed by Kwok et al.<sup>194</sup>. In comparison to omnivorous diets, vegetarian diets were associated with a significant reduction of IHD mortality (-25%; 95% CI: 0.68 - 0.82,  $P < 0.001$ ,  $I^2 = 35\%$ ); but not with a significant one on the reduction of mortality from CerVD (-7%, 95% CI: 0.78 - 1.10;  $P = 0.39$ ,  $I^2 = 44\%$ ) or from CV mortality (-7%, 95% CI: 0.86 - 1.00,  $P = 0.07$ ,  $I^2 = 0\%$ ). Similar limitations to that expressed by Kwok et al.<sup>194</sup> here above, need to be taken into account for the interpretation of the potential benefits of vegetarian diets on the CV risk.

Finally, it should be noted that the authors of these three meta-analyses did not perform a subgroup analysis specific to vegans. Consequently, the existing data do not permit a clarification of whether the benefits of vegan diets on CV mortality could be similar to those observed with vegetarian diets<sup>193-195</sup>.

Nevertheless, in order to attempt to determine the influence of a vegan diet on the risk of mortality attributed to CVD, the results observed in two prospective cohort studies published in 2013 (Orlich, SDA) and in 2016 (Appleby, non-SDA) are clinically relevant<sup>41,196</sup>.

As shown by Orlich et al.<sup>196</sup> in **table 8-1** from the Adventist Health Study-2 (n=73'308, follow-up = 5.6 yr.), strong diverging results were obtained for the total CVD and IHD mortality risks between men and women following vegan diets, with men showing a significant decrease, whereas a non-significant risk increase was observed among women.

A vegan diet is associated with a significant lower mortality risk (CVD and IHD), when compared to other vegetarian diets in men. Very diverging results are observed in women, both when compared with men, but also when comparing the different diets. For the whole group (men and women pooled), a vegan diet is not associated with a more favourable outcome than other diets.

**Table 8-1 Hazard ratio for overall cardiovascular and specifically IHD mortality as a function of the type of vegetarian diet in comparison to omnivores of the “Adventist Health Study 2”<sup>196</sup>**

	Women (n= 48'203)		Men (n= 25'105)		Total women and men	
	CVD total	IHD	CVD total	IHD	CVD	IHD
<b>Vegans (n= 5'548)</b>	+ 18%, ns (CI 95%: 0.88 - 1.60)	+ 39%, ns (CI 95%: 0.87 - 2.24)	<b>- 42%, s (CI 95%: 0.38 - 0.89)</b>	<b>- 55%, s (CI 95%: 0.21 - 0.94)</b>	- 9%, ns (CI 95%: 0.71 - 1.16)	- 10%, ns (CI 95%: 0.60 - 1.33)
<b>Ovo-lacto-vegetarians (n=21'177)</b>	- 1%, ns (CI 95%: 0.81 - 1.22)	- 15%, ns (CI 95%: 0.59 - 1.22)	<b>- 23%, s (CI 95%: 0.59 - 0.99)</b>	- 24%, ns (CI 95%: 0.52 - 1.12)	- 10%, ns (CI 95%: 0.76 - 1.06)	- 18%, ns (CI 95%: 0.62 - 1.06)
<b>Pesco-vegetarians (n=7'194)</b>	- 10%, ns (CI 95%: 0.66 - 1.23)	<b>- 49%, s (CI 95%: 0.26 - 0.99)</b>	<b>- 34%, s (CI 95%: 0.44 - 0.98)</b>	- 23%, ns (CI 95%: 0.43 - 1.30)	- 20%, ns (CI 95%: 0.62 - 1.03)	<b>- 35%, s (CI 95%: 0.43 - 0.97)</b>
<b>Semi-vegetarians (n=4'031)</b>	- 7%, ns (CI 95%: 0.64 - 1.34)	+ 9%, ns (CI 95%: 0.60 - 1.98)	- 25%, ns (CI 95%: 0.43 - 1.32)	- 27%, ns (CI 95%: 0.33 - 1.60)	- 15%, ns (CI 95%: 0.63 - 1.16)	- 8%, ns (CI 95%: 0.57 - 1.51)
<b>Total Vegetarians (n= 37'950)</b>	- 1%, ns (CI 95%: 0.83 - 1.18)	- 12%, ns (CI 95%: 0.65 - 1.20)	<b>- 29% s (CI 95%: 0.57 - 0.90)</b>	<b>- 29% s (CI 95%: 0.51 - 1.00)</b>	- 13%, ns (CI 95%: 0.75 - 1.01)	- 19%, ns (CI 95%: 0.64 - 1.02)

Analyses of mortality were performed using Cox proportional hazards regression adjusted for different age, sex and race. Statistical significance: s = significant (in boldface), ns: not significant

The analysis of both Oxford Vegetarian Study and EPIC-Oxford study performed by Appleby et al.<sup>41</sup>, (n=60'310, follow-up > 15 y.), show in **table 8-2** that vegans (men and women combined) have a non-significant slight decreased hazard ratio for IHD mortality (-10%, non-significant) among vegans when compared to non-vegetarian diets, as also seen with the Adventist study (**table 8-1**). When comparing the results between the two studies it is apparent that several results are in discordance, both in the risk tendency and the significance.

These diverging findings could be explained largely by the non-comparable lifestyles and dietary habits practiced by the various dietary groups of the American Adventist cohort and those of the two British cohorts, but are compatible with the meta-analysis by Kwock et al (**figure 8-6**).

The non-significant risk increases observed in the British cohorts for CerVD and CVD mortality, for vegan and some other vegetarian diets, are in contradiction with the frequently reported significant benefits of a vegan / vegetarian diets<sup>6,129,150,193,195,197</sup>.

**Table 8-2 Hazard ratio\* of cardiovascular mortality according to the type of vegetarian diet compared to non-vegetarian diets of the "Oxford Vegetarian Study & the EPIC-Oxford Cohort"<sup>41</sup>**

	Ischaemic Heart disease	Cerebrovascular disease	Cardiovascular disease
<b>Vegans</b> (n = 2'228)	- 10%, ns (CI 95% : 0.53 - 1.55)	+ 61%, ns (CI 95% : 0.97 - 2.69)	+ 21%, ns (CI 95% : 0.88 - 1.66)
<b>Pesco-vegetarians</b> (n = 8'516)	+ 6%, ns (CI 95% : 0.79 - 1.42)	+ 36%, ns (CI 95% : 0.99 - 1.87)	+ 26%, s (CI 95% : 1.05 - 1.51)
<b>Semi-vegetarians (n = 13'039)</b>	-4%, ns (CI 95% : 0.78 - 1.19)	- 12%, ns (CI 95% : 0.68 - 1.14)	-2%, ns (CI 95% : 0.85 - 1.13)
<b>Vegetarians (without vegans)</b> (n = 18'096)	+ 4%, ns (CI 95% : 0.83 - 1.30)	+ 15%, ns (CI 95% : 0.88 - 1.50)	+ 12%, ns (CI 95% : 0.96 - 1.30)
<b>Total vegetarians</b> (n= 41'879)	+3%, ns (CI 95% : 0.82 - 1.28)	+ 19%, ns (CI 95% : 0.91 - 1.54)	+ 13%, ns (CI 95% : 0.97 - 1.30)

\* Estimated by Cox Proportional hazards ratio regression adjusted for different risk factors. Statistical significance: s: significant, ns: not significant

In conclusion, the data presented in these different systematic reviews and meta-analyses of observational studies suggest that vegan and vegetarian diets could be associated with a lower risk of IHD mortality, but possibly not in vegan women.

Further investigation is needed, before recommending such types of diets for the general population, as a CVD preventive measure, in particular for women. In fact, the current scientific evidence does not support the favourable statements published recently to promote vegetarian and vegan diets<sup>6,107,150,198</sup>. In addition, it should be noted that vegan diets are not specifically listed in the recommendations for the prevention and management of cardiovascular diseases and their risk factors<sup>175,176</sup> on this topic by different authors involved in the Physicians Committee for Responsible Medicine promoting vegetarian and vegan diets<sup>6,198</sup>.

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## Amendment to the 2006 report

The recent data studying the association between vegan diets and cardiovascular health relativize the benefits of general vegetarian diets on reduction of the cardiovascular mortality cited in the previous report, which did not contain data on vegan diets.

There still are no specific studies investigating of vegan diets for the **prevention** of CVD. 2 cohort studies suggest that vegetarian diets could lower the risk of hospitalization for IHD, but not for CerVD.

Two cross-sectional cohort studies investigating the association of vegan diets and **IHD mortality** show a similar non-significant risk reduction (-10%). A stratification by sex in the SDA study shows however a non-significant risk increase for women (+39%), contrasting with a significant risk decrease for men (-55%).

In these studies, contradictory results were observed for total **CVD mortality**, when comparing the SDA study (-9%) and the non-SDA study (+21% risk), both non-significant. Further contrasting results were observed in the SDA study when stratifying the data by sex: +18% risk (non-significant) for women, and -42% (significant) for men.

One study reported a non-significant risk increase (+61%) for **CerVD mortality**.

In regard to the discrepancies of these results, possibly due to methodological limitations, further research is necessary before recommending vegan diets to prevent the morbidity and the mortality of CVD in the general population, namely for women.

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## 8.4 Cancer

**Lead author: Roger Darioli**

According to the Swiss Cancer Report 2015<sup>199</sup>, approximately 20'800 men and 17'650 women develop cancer each year. Cancers of prostate, breast, colorectal and lung account for slightly more than half of the cases. Moreover, cancers are not only the second cause of death but they represent also the greatest number of years of potential life lost through death before 70 years of age. Although there are multiple causes of cancer, the scientific literature considers that there is an increased risk of the most frequent cancers such as breast, prostate, and colon in connection with body fat excess, high consumption of red and processed meats and alcohol. Conversely, a diet high in fiber, fruits and vegetables could have a protective effect. Consequently, the recommendations of the Swiss League against Cancer advocate a balanced diet, rich in fruits and vegetables and poor in animal foods<sup>200</sup>. The aim of this review is to update scientific knowledge on the influence of vegan diets on cancer prevention between 2007 and December 2017.

### 8.4.1 Cancer incidence

During the last decade, only Dinu et al.<sup>195</sup> have performed a systematic review and a meta-analysis, which included cross-sectional and cohort studies, to evaluate the association between vegan or vegetarian diets and cancer incidence resp. mortality. With regard to incidence of total cancer, meta-analytic pooling under a random-effects model showed a significant lower risk of cancer among vegans (-15%; 95% CI: 0.75 - 0.95) and among vegetarians (-8%; 95% CI: 0.87 - 0.98) in comparison to omnivorous diets (**table 8-3**).

In the meta-analysis of Huang T et al.<sup>193</sup>, combined vegetarian and vegan diets were also associated with a significant lower risk of all-cancer (-18%; 95% CI: 0.67 - 0.97;  $I^2 = 27\%$ ) when pooling 7 prospective cohort studies, but the relative risk varied from -50% to + 12% in these studies.

To further examine the potential benefits of vegan diets on cancer incidence the results of the 5 large prospective cohort studies were published between 2007 and 2017, **table 8-3** also presents also a comparison

between the differences in incidence of all-cancer and site-specific cancers, by type of diet and gender  
195,197,201-209

Overall, vegans experienced modest risk reductions of incidence of all-cancer, either in the Adventist Health Study 2 (-14%; 95% CI: 0.73 - 1.00) or in the Oxford Vegetarian Study & EPIC-Oxford Cohort (-18%; 95% CI: 0.68 - 1.00). No significant association was found between a vegan diet and the different specific cancer sites. For **colon-rectum cancer** conflicting results were observed between the Adventist Health Study 2 (-14%; 95% CI: 0.59 - 1.24) and the Oxford Vegetarian Study & EPIC-Oxford Cohort (+31%; 95% CI: 0.82 - 2.11). In addition, in this later cohort study vegans have shown a significant higher risk of incidence of urinary tract cancers (+73% 95% CI: 1.05 - 2.84). In comparison with vegan diets, vegetarian diets showed similar trends, but with divergent results between the different cohort studies.

When the data were analyzed by gender, among vegan **women**, there was no significant risk reduction in incidence of all-cancer (-9%; 95% CI: 0.75 - 1.11), female cancers (-29%; 95% CI: 0.50 - 1.01) and breast cancer (-17% to -8%), but data are lacking for other specific sites of cancers. Among vegetarians, similar observations were made for the various types of cancer. However, opposite and non-significant results were shown for **breast cancer**, ranking from -30% to +14% in the cohort studies analyzed. Dinu et al.<sup>195</sup> reported also in their meta-analysis a small and non-significant reduction of this risk ratio (-6%, 95% CI: 0.84 - 1.06). In addition, vegetarian women experienced a significant increase of cervix cancer (+108%; 95% CI: 1.05 - 4.12).

Among **men**, vegan diets were also associated with a small and non-significant risk reduction in incidence of all cancers (-19%, 95% CI: 0.57 - 1.17), male cancers (-19%, 95% CI: 0.64 - 1.02). In contrast, prostate cancer incidence was significantly lower (-34%, 95% CI: 0.50 - 0.87) in the Adventist Health Study-2<sup>196</sup>, but that was not the case in the Oxford Vegetarian Study & EPIC-Oxford Cohort (-39%, 95% CI: 0.31 - 1.20)<sup>41</sup>. When looking at vegetarian men, conflicting results were observed between the two cohort studies analyzing the risk of prostate cancer incidence (-13% and +9%), thus leading to the conclusion that there is only limited evidence for a decreased risk for prostate cancer, as also concluded in the 2014 WCRF report<sup>210</sup>.

Finally, the differences by diet groups and by gender found for specific causes of cancer incidence merit further investigation.

In conclusion, there is a very small number of available vegan studies, with limited number of cases of cancers in some cohort studies, a large range of follow-ups, the already explained methodological limitations of these observational studies, leading to conflicting results. Further research is still required to prove the potential benefits of vegan diets to lower the risk of cancer incidence, and to demonstrate their advantages over the vegetarian and other plant-diets.



**Table 8-3: Comparative relative risk of cancer incidence by sites, type of diet and sex in the prospective cohort studies in comparison to non-vegetarian diets** 195,197,201-209

Authors	Study for cancer incidence	Sites of cancer	Follow-up (yr)	Person at-risk (n)	Cases (n)	Type of diets (vs. non vegetarian diets)		
						Ovo-lacto-vegetarian	Vegan	Vegetarian
						DRR, RR, HRs or SIR (95% CI)		
Males & Females cancers								
Dinu M et al., 2017	Meta-analysis of 3 cross-sectional studies and 2 prospective cohort studies	All sites	nd	38'033	nd	NR	0.85 (0.75 - 0.95)*	0.92 (0.87 - 0.98)*
Key TJ et al., 2009	Oxford Vegetarian Study & EPIC-Oxford Cohort	"	12.2	53'004	3'033	NR	NR	0.88 (0.81 - 0.96)*
Tantamango-Bartley Y et al., 2013	Adventist Health Study 2	"	4.1	93'777	4'007	0.95 (0.86 - 1.04)	0.86 (0.73 - 1.00)	0.92 (0.85 - 1.00)
Key TJ et al., 2014	Oxford Vegetarian Study & EPIC-Oxford Cohort	"	14.9	53'035	4'778	0.90 (0.84 - 0.97)	0.82 (0.68 - 1.00)	0.90 (0.93, 0.96)
Key TJ et al., 2009	Oxford Vegetarian Study & EPIC-Oxford Cohort	Brain	12.2	53'004	70	NR	NR	1.25 (0.72 - 2.16)
Key TJ et al., 2014	"	"	14.9	53'035	83	NR	NR	1.31 (0.79, 2.17)
Key TJ et al., 2009	"	Colorectum	12.2	53'004	353	NR	NR	1.12 (0.87 - 1.44)
Key TJ et al., 2014	"	"	14.9	53'035	536	1.01 (0.81 - 1.25)	1.31 (0.82 - 2.11)	1.04 (0.84, 1.28)
Orlich MJ et al., 2015	Adventist Health Study 2	"	7.3	65'577	490	0.83 (0.66 - 1.05)	0.86 (0.59 - 1.24)	0.79 (0.64-0.97)
Gisling A et al., 2015	Netherlands Cohort Study – Meat Investigation Cohort	"	20.3	10'210	437	NR	NR	0.89 (0.58 - 1.39)
Key TJ et al., 2009	Oxford Vegetarian Study & EPIC-Oxford Cohort	Stomach	12.2	53'004	47	NR	NR	0.36 (0.16 - 0.78)
Key TJ et al., 2014	"	"	14.9	53'035	64	NR	NR	0.38 (0.20, 0.71)
Key TJ et al., 2009	"	Upper gastro intestinal tract	12.2	53'004	74	NR	NR	0.81 (0.45 - 1.46)
Key TJ et al., 2014	"	"	14.9	53'035	123	NR	NR	0.93 (0.61, 1.43)
Tantamango-Bartley Y et al., 2013	Adventist Health Study 2	Gastro intestinal tract	4.1	62'274	495	0.76 (0.61 - 0.94)*	0.80 (0.55 - 1.17)	0.77 (0.63 - 0.93)*
Key TJ et al., 2009	Oxford Vegetarian Study & EPIC-Oxford Cohort	Lung	12.2	53'004	157	NR	NR	1.11 (0.75 - 1.65)
Key TJ et al., 2014	"	"	14.9	53'035	224	NR	NR	1.09 (0.78 - 1.53)
Gisling A et al, 2016	Netherlands Cohort Study – Meat Investigation Cohort	"	20.3	9'494	279	NR	NR	0.86 (0.40 - 1.85)
Tantamango-Bartley Y et al., 2013	Adventist Health Study 2	Respiratory tract	4.1	62'274	170	0.85 (0.61 - 1.30)	0.59 (0.28 - 1.23)	0.75 (0.54 - 1.04)
Key TJ et al., 2014	Oxford Vegetarian Study & EPIC-Oxford Cohort	Lymphatic/hematopoietic tissues	14.9	53'035	363	NR	NR	0.64 (0.48 - 0.84)*
Tantamango-Bartley Y et al., 2013	Adventist Health Study 2	Urinary tract	4.1	62'274	194	1.13 (0.79 - 1.61)	1.73 (1.05 - 2.84)*	1.21 (0.89 - 1.65)
Females cancers								
Dinu M et al., 2017	Meta-analysis of 3 cross-sectional studies and 2 prospective cohort studies	Breast	nd	24'789	nd	NR	NR	0.94 (0.84 - 1.06)
Travis RJ et al., 2008	EPIC-Oxford Cohort	- all ages	7.4	37'643	585	NR	NR	0.91 (0.72 - 1.14)
"	"	- pre-menopausal	"	26'509	290	NR	NR	0.95 (0.68-1.32)
"	"	- post-menopausal	"	11'134	196	NR	NR	0.79 (0.54 - 1.16)
Key TJ et al., 2009	Oxford Vegetarian Study & EPIC-Oxford Cohort	- all ages	12.2	39'064	891	NR	NR	0.91 (0.77 - 1.08)
Cade JE et al., 2010	UK Women's Cohort Study	"	9.0	28'442	677	NR	NR	0.88 (0.69 - 1.11)
"	"	- pre-menopausal	"	13'174	269	NR	NR	0.92 (0.67 - 1.24)
"	"	- post-menopausal	"	15'268	408	NR	NR	0.85 (0.58 - 1.25)
Key TJ et al., 2014	Oxford Vegetarian Study & EPIC-Oxford Cohort	- all ages	14.9	39'075	1'252	0.96 (0.84 - 1.10)	0.91 (0.61 - 1.34)	
Gisling A et al, 2016	Netherlands Cohort Study – Meat Investigation Cohort	"	20.3	4'906	312	NR	NR	0.70 (0.43 - 1.14)
Pennicook-Sawyers JA et al., 2016	Adventist Health Study 2	"	7.8	50'404	892	1.08 (0.92 - 1.27)	0.84 (0.62 - 1.13)	1.00 (0.87 - 1.16)
"	"	- pre-menopausal	"	15'597	164	0.98 (0.64 - 1.48)	0.86 (0.40 - 1.82)	1.14 (0.81 - 1.61)
"	"	- post-menopausal	"	34'807	728	1.10 (0.92 - 1.31)	0.83 (0.60 - 1.16)	0.97 (0.83 - 1.14)
Key TJ et al., 2009	Oxford Vegetarian Study & EPIC-Oxford Cohort	Cervix	12.2	39'064	40	NR	NR	2.08 (1.05 - 4.12)*
Key TJ et al., 2014	"	"	14.9	39'075	48	NR	NR	1.90 (1.00 - 3.60)
Key TJ et al., 2009	"	Endometrium	12.2	39'064	93	NR	NR	0.75 (0.45 - 1.28)
Key TJ et al., 2014	"	"	14.9	39'075	160	NR	NR	0.99 (0.67 - 1.45)
Key TJ et al., 2009	"	Ovary	12.2	39'064	132	NR	NR	0.69 (0.45 - 1.07)
Key TJ et al., 2014	"	"	14.9	39'075	204	NR	NR	0.87 (0.61 - 1.22)
Tantamango-Bartley Y et al., 2013	Adventist Health Study 2	All females cancers	4.1	40'129	801	1.04 (0.87 - 1.25)	0.71 (0.50 - 1.01)	0.97 (0.84 - 1.13)
Orlich MJ et al., 2015	"	Colorectum	7.3	42'212	305	NR	NR	0.79 (0.61 - 1.03)
Tantamango-Bartley Y et al., 2013	"	All sites	4.1	40'129	1'542	0.96 (0.85 - 1.08)	0.91 (0.75 - 1.11)	0.93 (0.84 - 1.03)
Males cancers								
Orlich MJ et al., 2015	Adventist Health Study 2	Colorectum	7.3	23'365	185	NR	NR	0.81 (0.58 - 1.12)
Tantamango-Bartley Y et al., 2016	"	Prostate	7.8	27'188	1'079	0.96 (0.83 - 1.12)	0.66 (0.50 - 0.87)	0.96 (0.83, 1.12)
Key TJ et al., 2009	Oxford Vegetarian Study & EPIC-Oxford Cohort	"	12.2	13'940	427	NR	NR	0.87 (0.64 - 1.18)
Key TJ et al., 2014	"	"	14.9	13'960	427	0.86 (0.66 - 1.11)	0.61 (0.31 - 1.20)	0.83 (0.64 - 1.06)
Gisling A et al, 2016	Netherlands Cohort Study – Meat Investigation Cohort	"	20.3	4'465	399	NR	NR	1.09 (0.68 - 1.76)
Tantamango-Bartley Y et al., 2013	Adventist Health Study 2	Males cancers	4.1	22'145	553	0.95 (0.66 - 1.25)	0.81 (0.57 - 1.17)	0.94 (0.42 - 2.07)
"	"	All sites	"	22'145	1'121	0.92 (0.80 - 1.06)	0.81 (0.64 - 1.02)	0.92 (0.81- 1.03)

NR = not reported; 95% CI = Confidence interval

DRR = death rate ratios; RR = risk ratio; HRs = Cox proportional hazards regression; SIRs = Standardized incidence ratios;

Statistically significant if DRR, RR, HR or SIR does not fall in the 95% CI



### 8.4.2 Cancer mortality

A collaborative analysis of data from the first 5 prospective studies, published in 1999 by Key et al. found no significant difference in death rates between vegetarians and non-vegetarians for cancers of the stomach, colon-rectum, lung, breast or prostate, but this analysis did not examine overall cancer mortality<sup>190</sup>. However, for vegans data are scarce<sup>194-196</sup>. The recent publication from Dinu et al.<sup>195</sup> in 2017 is the first systematic review and meta-analysis of observational studies performed to evaluate the association between the vegan and VGT diets and the risk of overall and specific cancer mortality. Otherwise, our review has included the Adventist Health Study-2<sup>196</sup> and the pooled Oxford Vegetarian Study & EPIC Oxford Study<sup>41</sup> in order to assess the consistency of the results between the two populations with different lifestyle habits.

As illustrated in **figure 8-7**, the meta-analysis of Dinu et al.<sup>195</sup> indicates that vegetarian diets including vegan diets were not associated with any significant decrease in the relative risk of mortality from all-cancer (-2%), colon-rectum (-10%), prostate (-10%), lung (-14%) or breast (-6%) in comparison with non-vegetarian diets. Separate analyses for breast cancer mortality exhibited a significant reduction in this risk for the SDA studies (-43%; 95% CI: 0.34 - 0.95), but in contrast, an almost significant increase of + 40% (95% CI: 0.98 - 2.01) for the non-SDA studies. Furthermore, a significant reduction of -41% (95% CI: 0.36 - 0.98) was found in studies with a duration < 14 year, this risk was not significantly increased (+ 38%; 95% CI: 0.82 - 2.30) if the duration was  $\geq$  14 years. The increased risk of this type of cancer among vegetarians included in the non-SDA studies or in the case of long duration studies remains unexplained. However, these findings require clarification by more specific research before long-term vegetarian diets can be recommended.

In the Adventist Health Study-2, a similar light and non-significant reduced risk of all-cancer mortality was associated with vegan and vegetarian diets when data for men and women were combined. However, divergent results were observed when results were stratified by sex.

Even if the relative risk of overall cancer mortality among vegetarians was the same in the Adventist Health Study-2<sup>196</sup> (-8%; 95% CI: 0.78 - 1.08) and in the Oxford Vegetarian Study & EPIC Oxford Study<sup>41</sup> (-9%; 95% CI: 0.80 - 1.03), vegans exhibited conflicting results (-8%; 95% CI: 0.68 - 1.24 versus +10%; 95% CI: 0.85 - 1.42). Moreover, the relative risk of mortality by specific cancers tended to increase in the UK cohort study among ovo-lacto-vegetarians and inversely to decrease in the meta-analysis from Dinu et al.<sup>195</sup> among the vegetarians. The data collected in the available observational studies are not sufficient to explain the discrepancies reported here. It must be recognized however that survival in individuals with diagnosed cancer depends on multiple factors, including the treatment modalities not taken into account in the presented studies. These methodological limitations lead to a C-level score of scientific evidence for recommendations<sup>12</sup>. No studies were found investigating the therapeutic impact of vegan or vegetarian diets for cancer survivors.

In conclusion, the scientific evidence available to date is still insufficient to consider whether vegan and vegetarian diets are associated with a significant reduction in risk of mortality by all cancers and mortality by specific cancers reported here; on the contrary Appleby et al.<sup>41</sup> show a non-significant increased mortality risk for breast cancer and other cancers, for pooled vegetarian diets. An overview of all studies is provided in **appendix III**.

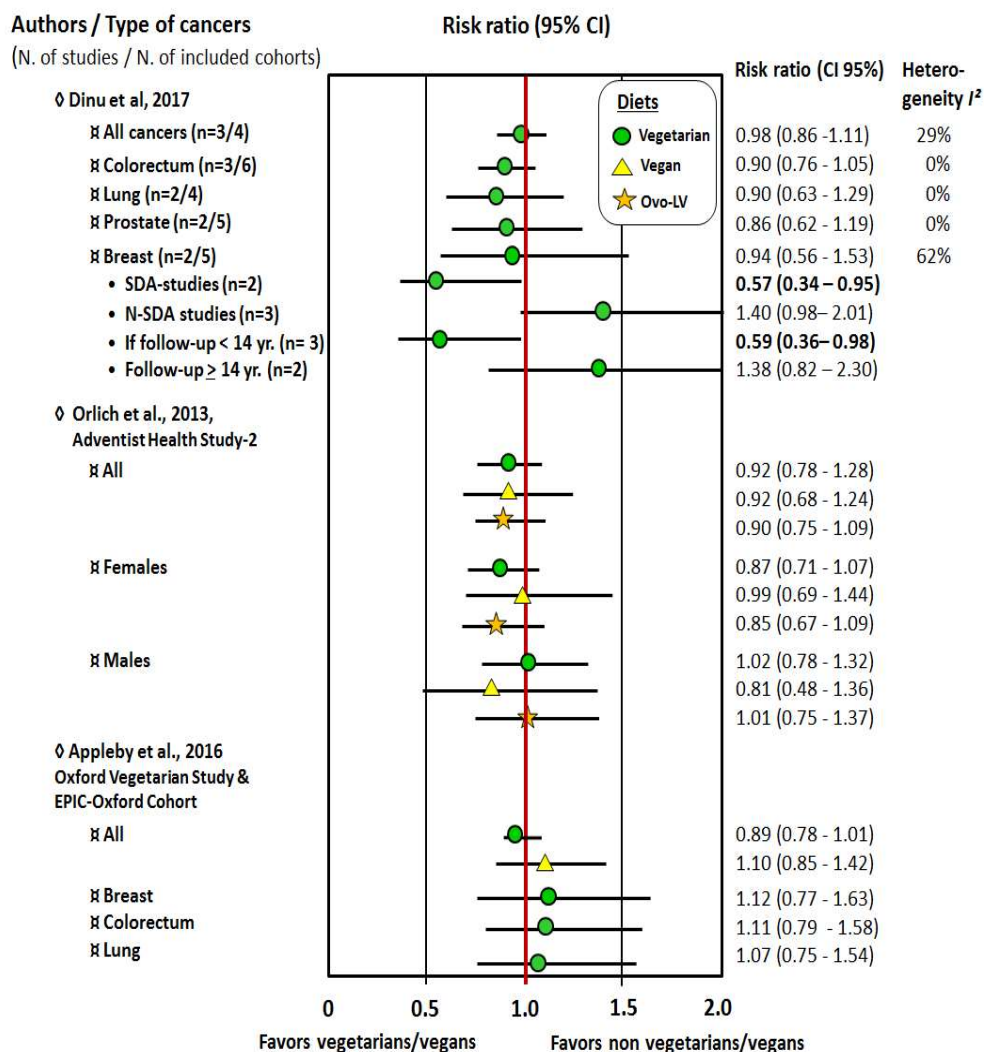


Figure 8-7: Risk ratio for cancer mortality and specific type of cancers according to the types of vegetarian diets as compared to non-vegetarian diets, Ovo-LV: ovo-lacto-vegetarian<sup>41,195,196</sup>

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## Amendment to the 2006 report

The previous report concluded that cancer incidence and mortality were lower among vegetarians than among non-vegetarians, with men benefiting rather more than women do. Vegan diets were not mentioned.

### Cancer Incidence

Recent data, derived exclusively from systematic reviews and meta-analyses of a small number of observational cohorts and cross-sectional studies, have shown that, in comparison with non-vegetarian diets, vegan diets were associated with a significant lower risk of all-cancer (-15%) when both sexes were pooled. Nevertheless, when stratifying the data some specific patterns arose.

- A non-significant lower risk was observed in the Adventist Health Study-2 for men (-19%) as well as for women (-9%).
- For specific cancer incidence, vegans exhibited divergent results, with a significant decreased incidence of prostate cancer (-34%) and a significant increased incidence of urinary tract cancer (+73%) in the same Adventist Health Study-2.

### Cancer Mortality

In contrast, the evidence available to date is still insufficient to confirm that vegan and vegetarian diets are associated with a significant reduction in risk of mortality by all cancers pooled.

Once again, Adventist studies and non-Adventist studies lead to partially contrasting results, for all cancers pooled, but in particular concerning breast cancer and colon-cancer. The meta-analysis of Dinu et al. also suggests that a longer follow-up (> 14 years) can increase the risk of breast cancer, contrasting with the significant reduction for breast cancer, observed with shorter follow-up (<14 years). These results challenge the expectations that a long-term plant-based diet would have a protective effect on these specific cancer forms.

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## 8.5 All-cause mortality

**Lead author: Roger Darioli**

Assuming that vegan diets are maintained for the long term, clearly their impact on major health outcomes such as total mortality requests should be indicated. Our review has identified only two prospective cohort studies (Orlich<sup>196</sup>, Appleby<sup>41</sup>) and the meta-analysis from Dinu et al. already mentioned above<sup>195</sup>.

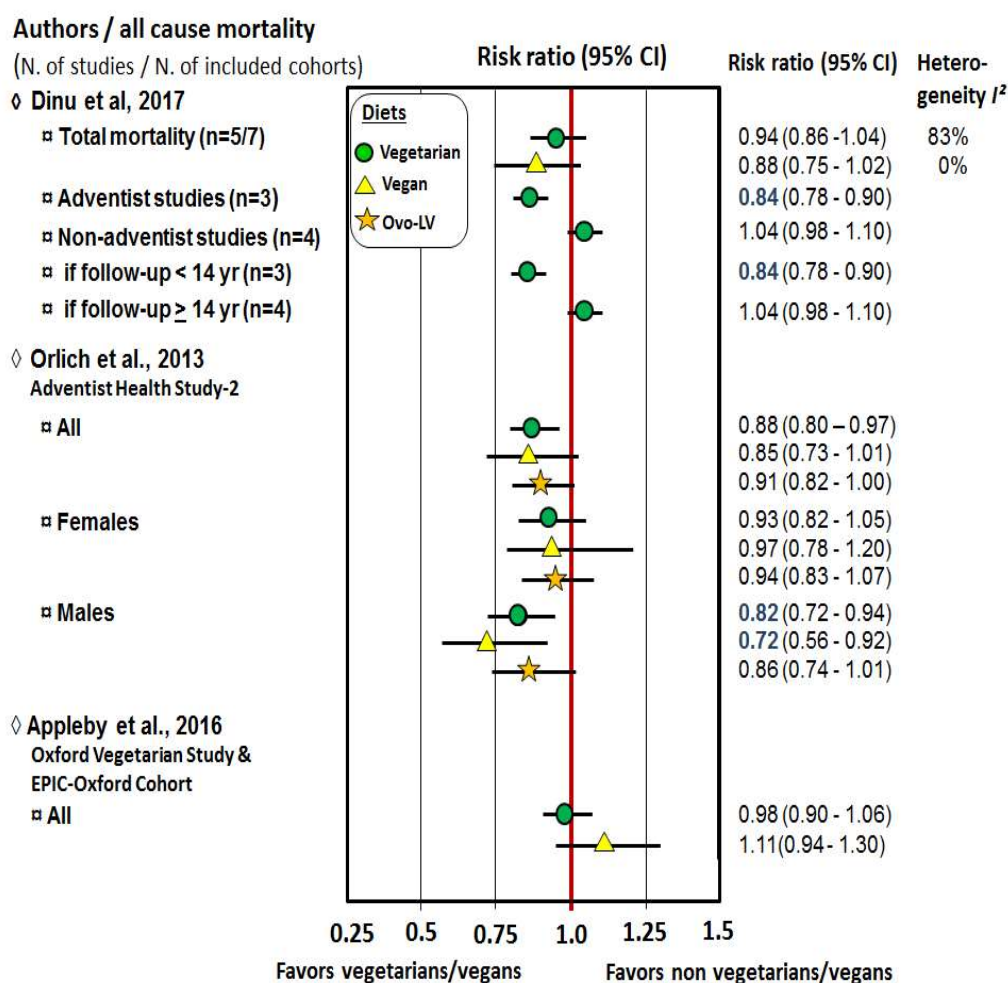
As illustrated in **figure 8-8**, vegans exhibited a non-significant reduced risk of total mortality (-12%; 95% CI: 0.75 - 1.02) as compared to non-vegetarian diets in the meta-analysis from Dinu et al.

A similar result was observed for vegan participants in the Adventist Health Study-2 (-15% CI: 0.73 - 1.01), however with differences between men (- 28%; 95% CI: 0.56 - 0.92, significant) and women (-3%; 95% CI: 0.78 - 1.20, non-significant)<sup>196</sup>. These results contrast with those seen among the vegans included in the Oxford Vegetarian Study & EPIC Oxford Study (+11 %; 95% CI: 0.94 - 0.30, non-significant), as compared to regular meat eaters<sup>41</sup>.

For the vegetarians, the meta-analysis from Dinu et al. shows contrasting results between the Adventist and non-Adventist studies, and between the studies with duration < or > 14 years<sup>195</sup>. Once again, as presented in the Adventist Health Study-2, vegan diets appear to have an increased protective effect in men, more than in women.

In a collaborative analysis of five prospective studies published in 1999, Key et al.<sup>190</sup> concluded that there were non-significant differences between vegetarians and non-vegetarians in all-cause mortality of 0.95

(95% CI: (0.82 - 1.11). Stratified by specific diets, a mortality ratio of 1.0 (95% CI: 0.70 - 1.44) was reported for the vegans and of 0.84 (95% CI: 0.74 - 0.96) for ovo-lacto-vegetarians excluding vegans.



**Figure 8-8: Risk ratio for all-cause mortality according to the types of VGT diets as compared to non VGT diets, ovo-LV: ovo-lacto-vegetarian**<sup>41,195,196 39, 192, 193</sup>

Such heterogeneity of risks remains unclear, based on the available data. Therefore, further research is necessary to determine whether vegan and vegetarian diets could reduce the risk of total mortality in comparison to non-vegetarian diets, independently of other healthier lifestyle choices.

In conclusion, due to the small number of studies with sufficient methodological quality and to the limitations of the studies reported here, the scientific evidence available to date is not sufficient to claim that vegan and vegetarian diets are associated with a significant reduction of total mortality. Moreover, these data suggest that vegan diets do not seem to provide advantages over other vegetarian diets. According to the importance of this issue, further research is required to confirm that long-term vegan or vegetarian diets can be associated with a significant reduction of all-cause mortality.

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## Amendment to the 2006 report

In the recent report, it was assumed that plant-based diets (rich in fruit, vegetables and nuts) were associated with a higher life expectancy. No specific data on all-cause mortality were included for vegan diets.

The recent data are derived from 1 systematic review and meta-analysis (including 7 cohort studies) and 2 single cohort studies suggest that the scientific evidence for an association between total mortality risk and vegan diets (including vegetarian diets) is inconclusive. Moreover, these data also suggest that vegan diets do not seem to provide advantages over other vegetarian diets. In view of the importance of dietary patterns for life expectancy, further research is necessary to assess the long-term effects of vegan vs. vegetarian vs. other diets on all-cause mortality.

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## 8.6 Vegan diets and other diseases

**Lead authors: Roger Darioli and Beatrice Baumer**

### 8.6.1 Bone frailty

Some concern has been expressed on the consequences of a long-term vegan diet on bone health, which in general decreases with age<sup>145</sup>. Long-term studies on the impact of a prolonged vegan diet on bone health are not (yet) available. However, possible risk factors could be calcium intake (and its bioavailability) and vitamin D status, as well as changes in the bone mineral density (BMD), already in younger vegans. A plant based diet could however also contain several bone-protecting constituents such as magnesium, potassium, vitamin K, and antioxidant and anti-inflammatory phytonutrients<sup>211</sup>.

BMD is frequently used as indicator of bone health. In a meta-analysis of the BMD of vegetarians in comparison to omnivores, mainly based on Asian case-control studies and with small number of participants, the authors conclude that vegetarians and especially vegans tend to have a significantly lower BMD but that „the effect size is unlikely to result in a clinically important increase in fracture risk“<sup>212</sup>. A major limitation of this meta-analysis of 9 case-control studies is however that age and duration of the vegan diet were not taken into account.

Lower and not significant BMD (including T and Z-scores) measurements were also observed by Knurick et al.<sup>213</sup> in 28 young vegans (average age 33.9 +/-8.6) as compared with 27 omnivores (average age 27.2 +/-6.7). Then vegan group had significantly lower potential renal acid load (PRAL). The authors also stress that these results cannot be extended to bone health with the ageing. Contradictory data on the BMD of vegans vs. vegetarians and omnivores could be explained by an incomplete assessment of various dietary factors, besides calcium and protein intake, e.g. the variability in the nutritional acid load, depending on the fruit and vegetable intake<sup>214</sup>. Conflicting statements show that the evidence of a protective effect of a diet with a low PRAL on bone health is not proved<sup>213,214</sup>.

Appleby et al. performed an analysis of the data from the EPIC-Oxford cohort study, comparing fracture rates between 1'026 vegan participants and 19'289 meat-eaters (during an average of 5.2 years of follow-up)<sup>62</sup>. The results show that vegans, when compared to meat eaters, exhibit a non-significant increased incidence rate ratio (IRR) for all bone fractures, with +15% (95% CI: 0.89 - 1.49) for both sexes combined, as well as for men +20% (95% CI: 0.73 – 1.98) and as for women +5% (95% CI: 0.76 – 1.44), when adjusted for confounding factors<sup>62</sup>.

The incidence rate ratio of a bone fracture was neutral (RR 1.00 (95% CI: 0.69 - 1.44), when comparing meat-eaters to a sub-group of vegans (n= 569), consuming at least 525 mg calcium / day (this also applies to other vegetarian diets). These authors conclude that *“the higher fracture risk among vegans appeared to be a consequence of their considerably lower mean calcium intake”*.

In the same study results for vegetarians (consuming dairy products) showed slightly lower, but non-significant, IRRs when compared to meat-eaters: +0.0% (95% CI: 0.89 - 1.13) for both sexes combined, as well as for men +1% (95% CI: 0.77 - 1.33) and as for women -2% (CI 95% CI: 0.85 - 1.12).

Interestingly, Tucker et al in their review have assessed the risks of low nutrients intakes for bone health and have given the description of possible sources of such critical nutrients for vegans <sup>211</sup>.

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### Amendment to the 2006 report

Although vegan diets include bone-protecting constituents, can decrease PRAL and urinary calcium, there is no evidence that these improve bone health, as stated in the previous report, derived from studies on the effects of a plant-based diet, but not necessarily vegan diets.

In 2 recent case-control studies a modest trend (significant in one study) towards a lower BMD, with a non-significant higher risk of fracture, was observed when comparing vegan diets to omnivorous diets.

The EPIC-Oxford cohort also showed a non-significant increase in incidence risk ratio for all bone fractures (+15%) predominantly among men, even after adjustment for multiple confounding factors (follow-up of 5.2 years on average). However, this risk was not increased among vegans consuming more than 525 mg calcium / day. In regard to the paucity of available data, more research is necessary to determine the long-term consequences of vegan diets on bone health.

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## 8.6.2 Irritable bowel syndrome

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder (FGID) worldwide. In Switzerland, IBS affects 5 to 20% of the adult population, with female predominance<sup>215</sup>. The pathophysiology of IBS is not completely understood, but several abnormalities appear to contribute to its pathogenesis, including dysregulation of the brain-gut axis, gut dysmotility, visceral hypersensitivity, low-grade mucosal inflammation, increased intestinal permeability and altered microbiota. Its aetiology is multifactorial and at least two thirds of patients with IBS relate their GI symptoms to the ingestion of specific foods<sup>216</sup>. Recent attention has been focused on FODMAPs (Fermentable Oligo-, Di-, and Monosaccharides, and Polyols, or oligo-, di- and mono-saccharides and fermentable polyols) which may tend to promote the emergence or exacerbation of IBS in persons sensitive to this functional colopathy<sup>217,218</sup>. On the other hand, fibers supplementation has recently been advocated to improve the symptoms of IBS<sup>219</sup>, but conflicting results were reported<sup>220-222</sup>. Typical dietary recommendations in IBS are focused mainly on what foods to avoid and such advices includes a reduce intake of insoluble fibres<sup>216,223,224</sup>. As vegan and vegetarian diets are characterised by increased dietary intakes of non-soluble fibres as well as plant-based foods rich in FODMAPs, some particular features related to vegan and vegetarian diets could worsen or improve IBS symptoms.

The available scientific data on this topic remain scarce, with only 3 recent publications comparing vegetarian diets to omnivorous diets.

In the cross-sectional data analysis of the Australian Longitudinal Study on Women's Health 9'113 women (aged 22–27 years), Baines et al.<sup>225</sup> reported significant higher rates of constipation or other bowel problems among vegetarians (22.7 %) than non-vegetarians (29.1 %,  $p < 0.001$ ).

A cross-sectional study performed by Ghoshal et al.<sup>226</sup> among 2'774 subjects in a rural Indian population found that participants with a predominantly vegetarian diet were more at risk for IBS (adjusted OR = 10.77, 95% CI: 1.49 to 77.89) than those with a non-vegetarian diet. However, due to the different methodological limitations of this study, namely the very large 95% CI, and the lifestyle habits of the participants, such results cannot be generalised to other populations.



The third paper by Buscail et al. is more appropriate for an assessment of the association between IBS and vegetarian diets in our country<sup>227</sup>. The NutriNet-Santé study is a web-based prospective observational cohort started in France in 2009 and still ongoing with 158'361 subjects enrolled at the time of the study. Among them, 41'908 subjects provided information on vegan and vegetarian diets before answering the FGID questionnaire. Participants were mainly women (78.0%) and the mean age was 49.8 +/-14.3 years. Overall 2'264 (5.4%) subjects reported an IBS, with a higher prevalence in women compared to men (5.6% vs 4.8%,  $P = 0.03$ ). Anyone who reported to be following a vegetarian/vegan diet at least once was considered as a vegetarian ( $n = 1'031$ ). Participants who declared at least 3 times that they followed a vegetarian/vegan diet (either at baseline or throughout the yearly follow-up questionnaires in NutriNet-Santé) were considered as stable vegetarians ( $n = 131$ ).

The multivariate analyses by logistic regression models adjusted for age, educational level, total energy intake, income level, smoking status, BMI, physical activity and gender has shown a non-significant trend of higher risk of IBS (odds ratio = 1.24, 95% CI: 0.95 to 1.62) among the vegans/vegetarians. This risk was significantly higher among the small number of stable vegan/vegetarians (odd ratio = 2.66, 95% CI: 1.51 to 4.68). According to the limitations of their cross-sectional NutriNet-Santé cohort, namely the definition of the vegan/vegetarian group and the small number of stable vegetarians, these authors concluded, *"this study suggests that a long term vegetarian diet could be associated with IBS. Nevertheless, further studies are needed to confirm these results, and investigate the multiple aspects of the vegetarian diet, possibly related to the IBS"*.

In summary, in agreement with Buscail et al.<sup>227</sup> further research is required to clarify whether vegan and vegetarian diets are susceptible to positively or negatively influence the emergence and intensity of symptoms related to IBS. Various web sites<sup>217,228,229</sup> contain information to help subjects with IBS who want to start or continue a vegan or vegetarian diet by further restricting it to fulfil low FODMAP requirements, but the effectiveness of this restricted dietary approach has not yet been established.

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### Amendment to the 2006 report

This topic was not discussed in the previous report. The existing data suggest a significant increase in IBS symptoms when following a vegetarian / vegan diets. Further research is required to investigate the effects of FODMAP-reduced vegetarian/vegan diets, which would then be very restricted diets, possibly linked to nutrient deficiencies.

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### 8.6.3 Fertility disorders

Improper diets and defective nutrition have been linked to a large number of diseases in humans<sup>230</sup>. Emerging evidence, however support lifestyle factors and nutrition as having impact on fertility<sup>231</sup>. Despite the considerable interest focused on vegetarian diets to improve health, the role of vegetarian diets rich in soy foods concerning male fertility remains unclear<sup>232</sup>. The concern lies in the fact that isoflavones in soy foods exert oestrogen-like effects on sperm in vitro and in-vivo, thus in bringing about the possible adverse effects of infertility and feminisation in men who consume soy products<sup>233</sup>. A study from 2008 concerning semen quality in 99 male partners of subfertile couples from an infertility clinic in Boston showed an inverse association between soy food intake during the three previous months and sperm concentration this remained significant after accounting for age, abstinence time, body mass index, caffeine and alcohol intake and smoking<sup>234</sup>.

To examine the effect of a life-long vegetarian diet on male fertility, Orzylowska et al.<sup>235</sup> of Loma Linda Adventist University in California carried out this study among members of the Seventh-day Adventist com-

munity living in the Loma Linda blue zone, a demographic area known for life longevity. The sperm characteristics of 26 ovo-lacto-vegetarians (mean age = 36.2.  $\pm$  1.1 years) and 5 vegans (mean age = 40.8  $\pm$  6.9 years) were compared to 443 non-vegetarian controls (mean age = 35.3  $\pm$  0.3 years). Overall, ovo-lacto-vegetarians had a significantly lower sperm concentration (50.7  $\pm$  7.4 million/ml) in comparison to non-vegetarians (69.6  $\pm$  3.2 million/ml). Furthermore, total motility was lower in the ovo-lacto-vegetarians (33.2  $\pm$  3.8% versus non-vegetarians 58.2  $\pm$  1.0%). Although vegans had a numerically lower concentration (51.0  $\pm$  13.1 million/ml) and lower total sperm motility (51.8  $\pm$  13.4%), these results were not statistically significantly different from non-vegetarians. The authors suggest that phytoestrogens and isoflavones in soy may be exerting a negative effect on sperm quality, but the data need to be carefully interpreted in light of the extremely small number of subjects studied, and effective phytoestrogen intake should be taken into account.

Case reports also exist which support a supplementation of phytoestrogens for promoting fertility in men<sup>236</sup>. Additional studies in which men were randomised to receive low or high doses of isoflavone supplementation to their diets found no significant differences in sperm parameters between the two groups<sup>237,238</sup>.

It has also been speculated that a lower fertility in general may be related to pesticide exposure, e.g. through fruit and vegetable consumption (see chapter 6.3). A recent study with patients of a fertility clinic (not focused on vegetarian diets) showed that the amounts of pesticide residues in non-organically produced fruits and vegetables were associated with lower total sperm counts and lower percentages of morphologically normal sperm<sup>239</sup>. Specific data linking vegan / vegetarian diets, pesticide residues and fertility were not found.

For women, the scientific literature is very scarce and of low scientific evidence. A 2014 Canadian observational study<sup>240</sup> provided a descriptive profile of self-reported lifestyle habits of 300 young women with infertility, the authors found that a high number of women reported past or present eating disorders (27.3%), vegetarian diets (26%, including 2% vegan). On older study by Pedersen et al.<sup>241</sup> studied 41 non-vegetarian and 34 vegetarian premenopausal women, included in two groups that were indistinguishable with respect to height, weight, body mass index, and menarche. The incidence of menstrual irregularity was 4.9% among non-vegetarians and 26.5% among vegetarians ( $P = 0.009$ ).

Overall, despite the paucity of available data, the results presented here suggest that long-term vegan and vegetarian diets could negatively affect fertility in males and in females. More research is clearly necessary to investigate the impact of a vegan diet and other lifestyle / environmental aspects on fertility. In the meantime, applying the principle of precaution, counselling on the possible consequences on their fertility should be given to young subjects wishing to adopt or maintain such diets.

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### Amendment to the 2006 report

The topic of fertility disorders was not discussed in the previous report. Due to the clinical relevance of this issue, the paucity of available data and the discrepancies between results, further research is required to elucidate the impact of vegan/vegetarian diets on fertility, and to deliver appropriate advices to young people interested in or choosing such diets.

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## 8.7 Mental diseases and eating disorders

**Lead authors: Roger Darioli and Beatrice Baumer**

### 8.7.1 Mental diseases

Mental diseases are a major public health concern, with 27% of the Swiss population concerned. 18.0% of the population have symptoms from moderate (13.4%) to high (4.6%) psychological distress. Depression and anxiety are the most common psychic illnesses, with women being more affected, and younger people more than older people<sup>242</sup>.

During the last decade, increasing knowledge has emerged about the effects of vegan and vegetarian diets on **physical health**, as seen in the previous chapters. However, little data is available on the associations between vegetarian (vegan included) diets and **mental health**. On a biological level, nutrition status resulting from vegan and vegetarian diets may affect brain processes relevant for onset and maintenance of mental disorders<sup>243-245</sup>.

Besides differences in nutrition status, vegetarians and non-vegetarians differ in a number of psychological and socio-demographic characteristics that may also influence their risk for mental disorders.

To date, no data have been reported on the potential risk of mental diseases related to vegan diets. Conflicting results, based mainly on cross-sectional studies, do not allow to conclude whether vegetarian diets (vegan diets included) are associated with positive or negative influences on mental health aspects such as mood, emotions, anxiety, depression<sup>225,246-250</sup>.

These discrepancies can result mainly from various methodological approaches, size and selection of populations, nutritional surveys and self-reported mental disorders.

The recent German report by Michalak et al.<sup>251</sup>, based on a prospective longitudinal study, can contribute to clarify this relevant clinical issue. 4'181 adults aged between 18 and 65 years were recruited between 1998 and 1999 in the German National Health Interview and Examination Survey and its Mental Health Supplement (GHS-MHS). This representative nationwide epidemiological study focused on major somatic and mental disorders, impairments, and healthcare utilization. In addition to physical assessments and comprehensive questionnaires about health-related behaviors and a nutrition survey, a standardized individual face-to-face diagnostic interview was performed by clinically trained interviewers (psychologists and physicians) to detect a broad spectrum of mental disorders.

In the sample, 1.3% (n = 54) of the participants were following exclusively vegetarian diets, 4.5% (n = 190) were on predominantly vegetarian diets, and 94.2% (n=3'872) non-vegetarians. The vegetarian participants were matched with socio-economical similar non-vegetarians (n= 242). Significant socio-economic factors were being age, age, sex, marriage status, community size, education).

A consistent pattern emerged with a gradual increase in prevalence of mental disorders over time, depending on the type of diets (see **table 8-4**). Higher odds ratios for anxiety and unipolar depression were associated with the degree of adherence to vegetarian diets when compared to the non-vegetarian matched sample. However, for somatoform disorders the extent of odd ratios was similar between the completely and completely /predominantly vegetarian groups.

Importantly, these authors indicate that “no evidence for a causal role of vegetarian diet in the etiology of mental disorders was found. Rather, the results were more consistent with the view that the experience of a mental disorder increases the probability of choosing a vegetarian diet, or that psychological factors influence both the probability of choosing a vegetarian diet and the probability of developing a mental disorder”.

**Table 8-4 Prevalence rates of mental disorders, by time sequencing, in the completely vegetarians, predominantly vegetarians, non-vegetarians (total and matched) samples<sup>251</sup>**

Mental disorders	Completely vegetarians	Predominantly vegetarians	Non-vegetarians (total sample)	Non-vegetarians (matched sample)	Comparison completely/ predominantly vegetarians vs. matched non-vegetarians	Comparison completely vegetarians vs. matched non-vegetarians
Time sequencing	(N=54)	(N=190)	(N=3'872)	(N=242)	OR (95% CI)	OR (95% CI)
<b>Unipolar Depressive Disorders</b>						
1-month	7.4%	6.8%	6.3%	5.0%	1.44 (0.67 to 3.07)	1.53 (0.48 to 4.95)
12-month	24.1%	14.7%	11.9%	10.3%	<b>1.75</b> (1.03 to 2.99)	<b>2.75</b> (1.30 to 5.82)
Lifetime	35.2%	25.8%	19.1%	20.7%	1.48 (0.98 to 2.26)	2.09 (1.10 to 3.95)
<b>Anxiety Disorders</b>						
1-month	20.4%	12.6%	10.7%	8.7%	1.76 (0.99 to 3.13)	<b>2.69</b> (1.12 to 5.99)
12-month	31.5%	9.5%	17.0%	13.2%	<b>1.87</b> (1.15 to 3.01)	<b>3.02</b> (1.52 to 5.98)
Lifetime	31.5%	22.1%	18.4%	15.3%	<b>1.77</b> (1.12 to 2.79)	<b>2.55</b> (1.30 to 4.99)
<b>Somatoform Disorders and Syndromes</b>						
1-month	9.3%	12.1%	7.8%	4.5%	<b>2.72</b> (1.32 to 5.60)	2.14 (0.71 to 6.44)
12-month	16.7%	17.9%	11.6%	9.5%	<b>2.04</b> (1.19 to .50)	1.90 (0.83 to 4.39)
Lifetime	25.9%	25.8%	16.9%	15.3%	<b>1.93</b> (1.23 to 3.03)	1.94 (0.96 to 3.91)

The relatively simple one-item measure of vegetarian diet and the small number of completely vegetarians presents a limitation to this cohort study. The socio-economic matching suggests that other risk factors are involved in the development of mental disorders.

In summary, despite the rarity of the scientific knowledge and the complexity of the mental disorders, the recent available data suggest that vegetarian diets could be associated with a higher risk of mental disorders. Due to the burden of mental disorders, well-designed intervention studies need to be performed to investigate possible causal patterns between vegan / vegetarian diets and mental disorders. These studies should take into account confounding psychological factors, which could affect both the choice of a vegetarian diet and the incidence of mental disorders, and possible nutrient deficiencies (e.g. vitamin B<sub>12</sub>, iron, iodine, long-chain PUFAs).

## Amendment to the 2006 report

Mental disorders were not specifically discussed in the previous report.

Despite inconclusive data based on the previous case-control studies, recent available European data suggest that vegetarian diets might be associated with a higher risk of mental disorders. However, further studies are needed to clarify this topic.

### 8.7.2 Eating disorders

Veganism shares some common aspects with restrained eating behaviours, thus leading to the question whether veganism can be associated with extreme forms of restrained eating, in particular eating disorders such as anorexia nervosa, bulimia, or binge eating. Research in this field is scarce, due to the low prevalence of people following a vegan diet and possible selection biases when recruiting participants for this type of study. The few recent studies are in general cross-sectional and are based on either assessing the prevalence of eating disorders in vegetarian / vegan subjects, or on assessing the dietary preferences of subjects diagnosed with eating disorders. All studies are performed with a limited number of participants and using different methodologies, thus making comparisons difficult. The limitations of these studies make it impossible to imply any causality. An overview of recent studies is summarized in appendix IV<sup>59,252-255</sup> D. The studies are difficult to compare, due to the heterogeneity in the approaches, not only in the classification of the diets (self-reported, or based on specific questionnaires), but also in the questionnaire batteries used to determine eating disorders.

The largest study with vegans was performed by Heiss et al. with a “Eating Disorder Examination” on vegans and omnivores (2 groups, n=358 vegans, n=220 omnivores, comparable in demographics, BMI, physical activity, smoking and drinking habits). The researchers observed a significantly lower risk for a pathological eating disorder in vegans<sup>252</sup>. Timko et al. also observed more eating disorders in semi-vegetarians, rather than vegans<sup>253</sup>. This issue of restrained eating in semi-vegetarians was also discussed by Forestell et al.<sup>256</sup>. These authors emphasize that correct classifications of diet, and of motivations (in particular the drive for thinness) are essential when investigating this topic.

Other studies, in particular those of Bardone-Cone et al., show that there was an association between eating disorders and vegetarianism (vegans were not specifically identified) in their sample. They also identified a weight-related reason for choosing a vegetarian diet<sup>254</sup>. Their results give some weight to the hypothesis mentioned in most articles, that vegetarianism / veganism might be chosen as socially acceptable ways to mask an eating pathology.

Any positive association between vegan diets and eating disorders would thus need more precise analysis; including detailed characterisation of the diets, data on dietary beliefs and eating habits, clear recruitment criteria and a sufficient number of participants. A longitudinal study would permit access to possible causation patterns, as the existing data are more oriented towards investigating whether a pre-existing eating disorder could lead to a vegan lifestyle; few data were found on investigating whether a vegan diet could lead to further dietary restrictions and with time to an eating disorder. In particular Robinson-O'Brien et al. observed that former adolescent vegans “may be at increased risk for extreme unhealthful weight-control behaviours”<sup>59</sup>.

A second group of studies in the field of mental health and veganism focused on the effect of diet on mood and stress. The mainly cross-sectional studies vary in the methodological approach and the studied populations and are therefore not comparable results are therefore not conclusive. An overview of some studies is provided by Beezhold et al.<sup>247</sup>

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### Amendment to the 2006 report

This topic was not mentioned in the previous report. Recent studies show contrasting results, possibly due to different methodological approaches. Further prospective studies, with appropriate designs, are necessary, in particular with younger population groups, and a longer follow-up might be required.

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## 9 Ethical considerations from the pediatricians

**Authors: Pascal Müller and Oswald Hasselmann**

A discussion on the far-reaching risks and benefits of an exclusion diet such as a vegan diet should include medical and ethical considerations, particularly so when children are involved. Within a culturally heterogeneous society, there is a wide variation in adopted lifestyles and associated diets. In industrialized western countries parents can choose almost any particular lifestyle for their family as long as the rights of others are not infringed. Parents respectively caregivers have the constitutional right to foster their child according to their own preferences. As autonomous person, they have the right to adopt a particular diet for themselves. If this diet is provided as the sole source of nourishment for the child, the long-term consequences for the dependent child should however be taken into account. Children have little choice in accepting or refusing the food that they are being offered. Consequently, their rights need to be protected by specific laws such as those formulated in the UN-Convention on the Rights of the Child.

Every child should ideally be fed according to accepted guidelines and age specific requirements. The individual likes and dislikes of the child for certain foods should be respected as far as the age specific minimal or maximal allowances for the different food components are met and are feasible within the means of a particular family. For the adolescent from the age of about 12 years until full legal maturity is reached the preference for a specific diet should be respected as long as the minor is not insisting on a diet, which in the opinion of the caregiver is clearly not appropriate. It remains difficult to generalize when a decision-making-competence for choosing a particular diet is reached. The adoption of a particular diet usually follows a multitude of reasons including emotional and idiosyncratic motives.

In the case of distinct food intolerance as in celiac disease or lactose intolerance or in the case of a child, suffering under anorexia nervosa medical guidelines should be followed. The use of coercion to accept a particular diet can only be accepted if the vital interests of a child at risk cannot be met otherwise as is the case for certain metabolic diseases.

A situation of child abuse should be considered if the caregiver, despite knowing better, enforces a diet upon the child, which according to mainstream opinion is deficient in essential nutrients.

Following a diet which has a proven detrimental effect on future health aspects, due to a too high concentration of certain food components such as fats or calories has been discussed in term of parental neglect. Any intervention by the State in such a case has so far been difficult to justify as there are no clearly defined thresholds above which one can speak of potentially irreversible harm when following a specific diet and due to the high regard for the autonomy of parents and the psychological well-being of the child as part of an interfered interfamily relationship.

A difficulty can arise when conflicting opinions about the pros and cons of a particular diet coexist at a particular point in time. From an ethical point of view, the autonomy of the parents has to be brought in line with the right of a particular child for an “open future” who knows that its interests will in the last resort be protected by State authorities.

Different health associations state that well-balanced and planned vegetarian and vegan diets are compatible with a healthy upbringing at all stages of fetal, infant, child and adolescent growth<sup>7,142</sup>. As there are no reliable studies on the long-term advantages and disadvantages of a vegan diet in early life, we do not recommend an animal product-exclusive vegan diet in the preschool period. The strain of offering an age appropriate diet with the right amount of micro- and macronutrients and the necessity of repeated laboratory examinations to continuously adapt the diet have to be balanced by a hypothetical gain in health quality and the respect for specific belief systems. As the child becomes increasingly more competent to make decisions for his/her own life and the organ systems have become well established, a vegan diet could, based on present knowledge, be followed at a later age to benefit from the positive health effects that have already been described for adults following a vegetarian or vegan life style. If a vegan diet is chosen for an infant

and child, we highly recommend that the diet will be accompanied by an advisory nutrition expert until a firm knowledge of possible dangers to a healthy development has been established.

## 10 Conclusions

The main objective of the present report was to provide an update on the scientific evidence for nutritional advantages and risks of a long-term vegan diet, namely its impact on health biomarkers, and on morbidity and mortality due to the major non-communicable diseases. The second objective was to evaluate whether a revision of the 2006 FCN nutritional recommendation for the Swiss population was necessary.

Our review has favoured larger primary studies (cross-sectional surveys, prospective cohorts, and randomized control studies) performed in Europe and USA as well as available meta-analysis and systematic review articles published after 2006 until December 2017.

There are now more data on the prevalence of vegetarianism and veganism in Switzerland, with 3 to 11 % of the adult population following a vegetarian diet and with approximately 0.38 to 3% for the adults following a vegan diet. These data confirm that vegetarianism is increasing, but that data on the prevalence of veganism are still unprecise.

Studies performed in Europe and the USA have shown that the ethical reasons (animal rights, ethics, spiritual beliefs, environment and non-specified other ethical reasons) were more commonly given as a reason for becoming vegetarian / vegan, than health reasons. This fact should be taken into account when addressing and communicating the necessity of planning a vegan diet.

### 10.1 Nutrient perspective

European studies with healthy adults, focusing on food intake data, show that vegan diets can generally cover the macronutrient needs. The average protein intake is adequate; the high variability in intakes suggests however that some subjects might not cover their protein needs. Qualitative data are lacking, this would be relevant to assess whether age-dependent needs in essential amino acids are covered.

Calculated dietary intakes show that deficiencies for micronutrients are possible; a limitation of this approach is that food composition databases do not always have full data sets for typical vegetarian or vegan food items.

Of particular concern is the observation that 10-50% of vegans do not take any supplements, in particular vitamin B<sub>12</sub>. Calculated micronutrient intake data, combined with appropriate serum and urine data, suggest that not only vitamin B<sub>12</sub> is deficient, but that other deficiencies be possible for some other micronutrients, in particular iodine, zinc, EPA and DHA fatty acids, as well as calcium.

Studies have shown that vegans do not consistently eat the recommended 5 daily portions of fruit and vegetables, this suggests that further investigations might identify different eating patterns among vegans, with possibly “healthier” patterns, corresponding to well-planned diets, and less planned diets, linked with higher deficiency risks.

Population groups with specific and more elevated nutrient needs than the general healthy adult population, are at higher risk of nutrient deficiencies, in particular during pregnancy and breastfeeding, as well as in infancy, childhood, and older age. Specific studies for these population groups are scarce, but nevertheless important, due to the vulnerability of these groups. Furthermore, particular attention should be taken when assessing nutrient needs for specific chronic diseases (e.g. debilitating chronic diseases, eating disorders, etc.), and if these can be adequately covered by well-planned vegan diets.

The different intake studies show that key elements of a well-planned vegan diet are: providing adequate energy, covering quantitative protein needs, consuming 5 portions of vegetable and fruit, consuming iodized salt, mandatory supplementation with vitamin B<sub>12</sub>, covering other macro- and micronutrient needs with an appropriate variety of food items, and supplementing for specific needs. Information about good sources for iron, zinc, calcium and n-3 fatty acids should be provided (food and/or supplements, and/or fortified food), as well as the consequences of selenium deficiency. Monitoring of these critical micronutrients is highly recommended.

## **10.2 Life cycle aspects**

### **10.2.1 Pregnancy and breastfeeding**

Research in this field has remained very scarce during the last decade. Pregnancy is linked with increased nutrient needs, with iron, iodine, zinc and vitamin D being critical, as well as selenium. These are also typically critical micronutrients in an average vegan diet, thus deficiency risks can be compounded by an injudicious vegan diet during pregnancy. Based on the current knowledge, a vegan diet cannot be recommended during the pregnancy. Data are lacking to prove the harmlessness (or even risks/benefits) of well-planned vegan diets, mainly for the foetus and the development of child. However, for pregnant women wishing to follow such a diet, medical supervision and counselling by a dietician might be necessary; in order to define a well-planned diet covering specific needs. In particular the vitamin B<sub>12</sub> and iodine status should be monitored and accordingly supplemented, see **table 11-1**.

More data are necessary to further investigate the health consequences not only for the mother, but also for the fetus, possible beginning in the preconceptional phase.

### **10.2.2 Infants and children**

A lack of data persists to know whether the nutritional requirements are covered and whether the development of children and adolescents fed with a vegan diet is secure. Therefore, more knowledge is required before recommending this type of diet in these age groups.

If a vegan diet is chosen for an infant and child, it is highly recommended that an advisory nutrition expert will accompany the diet until a firm knowledge of possible dangers to a healthy development has been established, see **table 11-1**.

### **10.2.3 Ageing**

The impact of a long-term vegan diet for older adults is still a field requiring more investigations to determine the specific needs according to the health status of such group of population and to investigate their risk of increased vulnerability in case of nutrient deficiencies. More evidence is necessary before recommending a vegan diet for older adults.

## **10.3 NCDs**

### **10.3.1 Cardiovascular diseases**

#### CV risk factors

Cross-sectional studies and prospective cohort studies have shown that vegan diets were associated with a lower risk for overweight/obesity, hypertension, hypercholesterolemia, high LDL-cholesterol, or type-2 diabetes.

Intervention studies demonstrated that vegan diets can induce a reduction of body weight in obese, and possibly reduce total cholesterol, LDL-cholesterol and HbA1c, however these results are comparable to other diets, namely to Mediterranean diet. Contradictory results were given for blood pressure.



There is therefore no solid evidence for prescribing such a diet, furthermore the restrictive character of vegan diets would not appeal to patients lacking the necessary intrinsic ethical or health-driven motivations, and thus limit a long-term adherence.

#### CVD prevention

Until now, no studies have been published on the possible benefits of a vegan diet in the primary prevention of ischemic cardiovascular diseases. However, recent data, based on only 3 cross-sectional studies, have shown a significant lower risk of hospitalization for or death from IHD among British vegetarians (32%), as well as among Danish vegetarian Seventh-day Adventists (-9%) and Baptists (-13%), when compared to the British non-vegetarians and to the general Danish population. There were no significant lower risk of hospitalization for CerVD in both Danish groups. More research is needed to investigate if similar results can be achieved with vegan diets.

#### CVD mortality

Two cross-sectional SDA and non-SDA studies have investigated the association between vegan diets and the mortality due to the different ischemic CVD, as compared to non-vegetarian diets. For total CVD mortality, markedly divergent results were noticed between the Adventist Health Study-2 and the pooled EPIC-Oxford studies for total CVD mortality (- 9% versus + 21%), as well as between men (- 42%) and women (+ 18%) in the SDA study, but not in the non-SDA study (- 10% for both men and women). For IHD mortality the reduction of risk was similar in both cohorts (- 10%, not significant). However, the risk of CerVD mortality, reported only in the SDA study, was much higher (+ 61%, not significant) for the vegans, when compared to regular meat eaters.

Diverging results have also been reported for vegetarian diets, when comparing SDA to non-SDA studies.

Further research, (in a European, non-SDA-context) is necessary to determine whether vegan diets could safely reduce the risk of CV morbidity and mortality, before vegan diets can be included in nutritional guidelines for the prevention of CVD in the general Swiss population.

### **10.3.2 Cancer**

#### Cancer incidence

The perusal of recent meta-analyses of 3 cohort studies showed that vegan diets were associated with a significant lower risk of all-cancer incidence (- 15%), in comparison with non-vegetarian diets. When stratifying the vegan data, a non-significant lower risk was observed in the Adventist Health Study-2 for men (- 19%) as well as for women (-9%). For specific cancer incidences, vegans exhibited divergent results, in particular with a significant decreased incidence of prostate cancer (- 34%) and a significant increased incidence of urinary tract cancer (+ 73%) in this SDA study. In addition, opposite and non-significant results were found for colorectum cancer between both SDA (-16%) and non-SDA Study (+ 31%).

Similar trends were observed for the vegetarian data reported, namely with a significant lower risk of prostate cancer incidence (-34%) only in the SDA study.

#### Cancer mortality

Data diverge when comparing all-cancer mortality risk data for vegan diets between SDA studies (-8 %) and non-SDA studies (+ 10%), when compared to the reference (non-vegetarian/vegan) participants, both results are however non-significant. A non-significant risk of all-cause cancer is also reported in the SDA study among men (- 19%) and women (- 1%), in contrast with the results obtained for vegetarian men (+ 2%) and women (- 13%).

For vegetarians, the meta-analysis of 4 cohort studies show a non-significant reduction in risk of mortality by all cancers pooled (-2%). Once again, SDA studies and non-SDA studies lead to partially contrasting results, in particular concerning breast cancer and colon-cancer. In addition, this meta-analysis suggests also that a longer follow-up (> 14 years) can increase the risk of breast cancer, contrasting with the significant reduction of this cancer, observed with shorter follow-up (< 14 years).

Overall these results challenge the expectations that a long-term vegan diet would have a protective effect on cancer incidence and mortality. Further research is needed to investigate the advantages and disadvantages of vegan / vegetarian diets on risk of all- and specific cancers, especially cancers under dietary influence. The duration of the diet should also be taken into consideration in these types of studies.

### 10.3.3 Total mortality

The previous report assumed that, on the basis of then available epidemiological studies, a plant-based diet (rich in fruit, vegetables and nuts) was associated with an increased life expectancy. No specific data on all-cause mortality were reported for vegan diets at the time.

The recent data based exclusively on the meta-analysis of Dinu et al has demonstrated a non-significant decrease of total mortality among vegans (-12%). However, divergent and non-significant results were observed in the SDA study (-15%) and in the non-SDA study (+11%). A stratification of risk by gender, reported only in the SDA study, has shown a significant decreased risk of total mortality among men (- 38%), but a non-significant decrease of - 3% among women.

Diverging results were also observed for vegetarians, when comparing the meta-analysis, and the separate results for SDA and non-SDA studies. Therefore, the scientific evidence available to date is not sufficient to claim that vegan and vegetarian diets are associated with a significant reduction of total mortality. Moreover, these data suggest that vegan diets do not seem to provide advantages over other vegetarian diets. In regard to the importance of this issue, further research is required to confirm that long-term vegan or vegetarian diets can be associated with a significant reduction of all-cause mortality, and with a longer healthy life expectancy.

### 10.3.4 Other NCDs

#### Bone frailty

In contrast to the previous report, the recent data, based only on 2 case-control studies, suggest that vegan diets can be associated with a modest trend towards a lower BMD and towards a non-significant higher risk of bone fractures, when compared to omnivorous diets. The EPIC-Oxford cohort<sup>60</sup> showed a non-significant increase of incidence risk ratio for all bone fractures (+15%) predominantly among men, even after adjustment for multiple confounding factors. However, this risk was not increased among vegans consuming more than 525 mg calcium / day. Due to the paucity of available data, more research is necessary to determine the long-term consequences of vegan diets on health bone, taking into account nutrient intakes, and evaluating potential bone-protecting constituents contained in a well-balanced vegan diet.

#### Irritable bowel syndrome

This topic was not discussed in the previous report. Vegan and vegetarian diets are characterised by increased intakes of non-soluble fibres, as well as of food items rich in FODMAPs, components that could exacerbate IBS symptoms. The existing data suggest that a significant increase in IBS symptoms is indeed possible when following vegetarian / vegan diets. However, further research is required to investigate the magnitude of this functional digestive disorder, as well as the effects of specific FODMAP-reduced vegetarian/vegan diets, which would then be highly restricted diets, with an increased risk of nutrient deficiencies.

#### Fertility disorders

Although improper diets and defective nutrition have been linked to a large number of diseases and disorders of the reproductive function in humans, this topic was not mentioned in the previous report. Overall, despite the paucity and the discrepancies of available data, the results presented here suggest that long-term vegan and vegetarian diets could negatively affect fertility in males and possibly in females. More research is clearly necessary to elucidate the impact of vegan / vegetarian diets on fertility, and to deliver appropriate advices to young people interested in or choosing such diets.



### Mental diseases

Mental disorders were not specifically discussed in the previous report. However, on a biological level, nutrient deficiencies ensuing from insufficiently planned vegan and vegetarian diets may affect brain processes relevant for onset and maintenance of mental disorders.

To date, no data have been reported on the potential risk of mental diseases related to vegan diets, besides some inconclusive data based on a small number of previous case-control studies. The recent available European data for vegetarian diets suggest that these could be associated with a higher risk of mental disorders, this leads to the conclusion that further studies are needed to clarify the impact of vegan diets on mental diseases, also taking into account the effective nutrient status.

### Eating disorders

Eating disorders, in particular extreme forms of restrained eating, such as anorexia nervosa, bulimia, or binge eating have not been frequently studied in connection with vegan diets. The few recent studies diverge in their conclusions, mainly due to their different objectives, study groups and methodological approaches. More longitudinal studies are necessary.

## 11 Final recommendations of the work group

### 11.1 Dietary guidelines

The current scientific evidence is too low to conclude that vegan diets are generally healthy diets, in particular concerning their long-term impact on the risk of several diseases and all-cause mortality. These diets can therefore not be recommended, in a disease prevention optic.

When people choose a vegan diet, their motivations are in general very strong, however these are not necessarily health-based convictions. Therefore, for such persons, evidence-based information and advice on well-planned vegan diets is necessary, as well as recommendations for follow-ups by health professionals, these recommendations are summarized in **table 11-1**.

The pillars of these recommendations should be a well-balanced diet, covering energy and macronutrient needs (in particular protein) and including 4-5 portions of fruit and vegetable per day, specific supplementations (or fortified food) and regular blood testing for specific nutrients (e.g. vitamin B<sub>12</sub>, iodine and others if pertinent), as well as specific biomarker controls by health professionals.

The working group suggests the development of a vegan dietary guideline could be helpful, in particular if it includes food items available in Switzerland. Models for these guidelines could be the Spanish approach<sup>8</sup>, the Harvard vegetarian/vegan diet pyramid<sup>257</sup>, or the British NHS recommendations<sup>258</sup>.

**Table 11-1 – Summary of recommendations and precautions per population groups wishing to follow a vegan diet**

Age group	Recommendation	Specific dietary recommendations & supplementations	Testing
<b>Pregnancy and lactation</b>	Not recommended	<ul style="list-style-type: none"> <li>• Strict precautions are needed for women who are highly motivated to adopt such a diet. A nutrition specialist should be involved, as well as clear information to the gynecologist.</li> <li>• Follow the German guidelines for general supplementations during pregnancy</li> <li>• use of iodized salt</li> <li>• folate supplements (preconceptionally)</li> <li>• according to test results: iron, B<sub>12</sub>, Vitamin D in risk groups</li> <li>• nutrition assessment for calcium, zinc and n3-fatty acids</li> <li>• Consider multivitamin tablet for supplementation</li> </ul>	Vitamin B <sub>12</sub> analysis* Hb, Ferritin, Vitamin D in risk groups TSH
<b>Infants</b>	Not recommended	<p>Exclusive breast feeding until 6 months Breast fed: according to laboratory analysis, B<sub>12</sub> supplementation (of mother and infant) Formula-fed: adapted soy-infant formula Solid food</p> <ul style="list-style-type: none"> <li>• A sufficient supply of protein sources covering all essential amino acids</li> <li>• Energy-dense solid food, containing with ALA-rich oil supplements (linseed, walnut or rapeseed)</li> </ul> <p>Supplement</p> <ul style="list-style-type: none"> <li>• iron (mainly in breast-fed infants after 6 months)</li> <li>• Vitamin K, Vitamin D as for all infants</li> <li>• Vitamin B<sub>12</sub></li> <li>• evaluate zinc and iodine intake</li> </ul> <p>Dietitian/pediatrician support (diet diary / lab controls)</p>	analysis of vitamin B <sub>12</sub> * (infant's and mother's blood) consider also zinc, vit D, <i>Quick</i> , ferritin, TSH
<b>Toddlers</b>	Not recommended	<ul style="list-style-type: none"> <li>• Check for energy intake (percentiles) developmental milestones and micronutrient intakes</li> <li>• Limit raw food (lower digestibility, difficult to ingest, caloric density)</li> <li>• Advise about grinding nuts (choking risk))</li> <li>• Check calcium intake (Ca-supplemented drinks, calcium rich mineral water)</li> <li>• Check iodine supplementation (salt)</li> <li>• Mandatory vitamin B<sub>12</sub> supplementation</li> <li>• Vitamin D as recommended for all toddlers</li> </ul> <p>Dietitian/pediatrician support (based on the analysis of 3-day dietary records / lab controls)</p>	analysis of vitamin B <sub>12</sub> * consider also zinc, vit D, <i>Quick</i> , ferritin, TSH
<b>Adolescents</b>	Not recommended (see ethical considerations, chapter 9)	Consider recommendations for adults with additional evaluation about motivation / eating disorders	Regular blood testing as in childhood (frequency to be discussed with the treating physicians)
<b>Healthy adults</b>	Acceptable for nutritionally well informed adults	<p>Elements of a well-balanced diet should take into account</p> <ul style="list-style-type: none"> <li>• Energy needs</li> <li>• Protein quantities and quality, giving examples of suitable quantities and combinations</li> <li>• Micronutrient supplementation resp. fortified food</li> </ul> <p>Although well-planned and supplemented vegan diets can cover nutrient needs there is currently no clear evidence for long-term health benefits</p>	Vitamin B <sub>12</sub> analysis* Regular blood testing of ferritin (frequency to be discussed with the treating general practitioner)
<b>Patients with diagnosed diabetes type 2 and/or cardiovascular diseases</b>	Acceptable for nutritionally well informed patients	<p>There is some evidence about possible metabolic benefits of self-chosen vegan diets (e.g. reduced risk for overweight/obesity, dyslipidaemia, HbA1c). It remains unclear whether vegan diets are more effective than other dietary therapeutic approaches to prevent type 2 diabetes or CVD, and to reduce the clinical complications related to these metabolic diseases or to prevent the recidivism of CV events.</p> <p>Nevertheless, for highly motivated subjects, adoption or maintenance of such diets need strict precautions as mentioned for adults.</p>	Disease-specific biomarkers, as well as nutritional status markers defined for adults here above.
<b>Special population groups, e.g., frail older adults, patients with debilitating diseases, persons with eating disorders</b>	Not recommended	<p>If a vegan diet is chosen, specific dietary and medical guidance is necessary, in addition to the nutrients supplementations defined for adults, here above.</p> <p>Nevertheless, for highly motivated subjects, adoption or maintain of such diets need strict precautions, as mentioned for adults, as well as medical supervision</p>	Disease specific biomarkers as well as nutritional status markers Vitamin B <sub>12</sub> analysis* Regular blood testing of ferritin frequency to be discussed with the treating general practitioner)

\*vitamin B<sub>12</sub> analysis (holoTCII / MMA in urine / Homocystein in serum /B<sub>12</sub> in plasma) in the specific subchapters (chapter 7)

## 11.2 Final recommendations and perspectives

- Guidance is necessary for making healthy choices, and planning an appropriate vegan diet. It would thus be advisable that societies endorsing vegan lifestyles (in particular the Swiss Vegan Society and Swissveg) would be involved in the development and diffusion of specific recommendations for this small population group. Other stakeholders should be invited to participate in this process, in particular the Swiss Society for Nutrition, dieticians, pediatricians, gynecologists etc.).
- Vegans should be encouraged to regularly check their nutritional status, in particular for vitamin B<sub>12</sub> (not only by measuring serum B<sub>12</sub> but also of holo-trans-cobalamin), as well as other vitamins, e.g. vitamin D, and other micronutrients (e.g. ferritin in women).
- It is important to fill the gaps for missing data in Switzerland regarding nutritional data on food items frequently consumed by vegans, as well as vitamin B<sub>12</sub> in fermented products, phytic and oxalic acid levels.
- Shifts in dietary patterns could also potentially increase the exposure to contaminants found mainly in plant-based products, e.g. pesticides and arsenic in rice. Such potential risks should be monitored.
- Future monitoring campaigns for generally critical micronutrients in the Swiss population (e.g. iodine, selenium) should include sample participants following a vegan diet. In addition eating behavior should be assessed.
- For further menuCH monitoring specific food items consumed by vegans should be taken into account. The Swiss food legislation should correct the definition of vegan food, excluding additives and processing aids of animal origin.
- More investigations are also necessary for younger population groups (mid-late teens), the prevalence data of 6% in the 15-34 age group should be verified, as well as motivations, eating behaviors and durations of a vegan diet. Possible associations with eating disorders should be carefully investigated.
- Due to the demographical shift towards an ageing population, the consequences of a prolonged (over decades) vegan diet are yet largely unknown. Possible health consequences (e.g. bone health and sarcopenia) in an ageing vegan cohort should be monitored / researched.
- More research might be needed on the influence of motivation (ethical, philosophic, political or health driven) for a vegan lifestyle and the impact on dietary patterns and use of supplements / fortified food or other fortified items (e.g. toothpaste).

## 12 Acknowledgements

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## 13 Conflicts of interest

No authors have reported a conflict of interest, with the exception of Diego Santini representing the Vegan Society Switzerland.

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# 15 Appendices

## Appendix I

Sources of macronutrient intake with a balanced omnivorous diet (for adult, low physical activity level), scenario-based calculation, based on dietary recommendations of the SGE and the Swiss nutrient database

food plant origin	quantity (g)	energy (kcal)	protein (tot g)	carbs (tot g)	fats (tot g)	food animal origin	quantity (g)	energy (kcal)	protein (tot g)	carbs (tot g)	fats (tot g)
3 portions vegetables, e.g. broccoli	360.0	90.0	1.1	8.3	1.4	1 portion milk, skimmed	200.0	66.0	6.8	9.4	0.0
2 portions fruit, e.g. apples	240.0	122.4	0.7	27.8	0.2	1 portion yoghurt, natural, unsweetened	150.0	106.5	6.0	8.3	5.4
1 portion bread, e.g. "Ruchbrot"	120.0	224.0	8.6	44.8	1.2	1 portion hard cheese, e.g. parmesan	20.0	76.2	7.2	0.3	5.1
1 portion egg-free pasta cooked	240.0	259.2	8.6	52.8	1.2	1 portion meat, e.g. beef steak	120.0	165.6	26.8	0.0	6.5
1 portion potatoes (cooked)	200.0	152.0	3.6	34.0	0.2	1 portion butter	10.0	74.6	0.1	0.1	8.2
nuts (unsalted, e.g. walnuts)	30.0	202.2	4.4	3.2	19.1						
oils 3 tablespoons (20 ml, e.g. canola)	60.0	539.4	0.0	0.0	45.0	1 snack, e.g. icecream (vanilla cream)	80.0	136.8	2.6	16.0	6.6
Total from food of plant origin	1250.0	1589.2	27.0	170.9	68.4	Total from food of animal origin	580.0	625.7	49.5	34.1	31.9
Total (both sources)	1830.0	2214.9	76.5	204.9	100.3						
% of plant origin	68.3	71.8	35.3	83.4	68.2						



## Appendix II

### Cross-sectional studies mentioned in chapter 6 – nutrient intakes

Study	Country	Study type	Scope of the study	Recruiting/ cohort	n	Age groups	Diets / reference / classification	Supplement use / fortified food	Diet duration	Anthropometric / nutritional assessments	Software / FCDB	Results / comments / limitations
Kristensen et al. <sup>40</sup>	Denmark	Observational study	effect of a strict vegan diet on microbiota	Local newspapers, online resources	75 vegans, age-range matched with 1627 non-vegan/vegetarians from the DANSDA	18-61	DANSDA-group (non vegan/non-vegetarian)	All nutrients noted, with daily dosage (vegan group)	Min 1 year	Weight / height measured, 4-day weighed food dairy (vegan group) DANSDA : food recording Calculation of average daily intake	Dankodt Pro software / Danish food composition databank	Calculated intakes for macronutrients and micronutrients
Elorinne et al. <sup>45</sup>	Finland	Cross-sectional	Compare dietary intake and nutritional status of Finnish long-term vegans and non-vegetarians	Finnish vegan association newspaper, online discussion forums (for vegans and non-vegetarians)	22 vegans, + 19 sex- and age-matched non-vegetarians	18-50	Non-vegetarians	In questionnaire	Min 1 year,	Three-day dietary records (after instruction) + Questionnaire on long-term eating habits	Finnish Nutrica software + Finnish FCDB	Food items intake (per food group) calculated nutrient intake Nutrient Biomarkers in plasma, serum, urine Polyphenols in plasma
Schüpbach et al. <sup>38</sup>	Switzerland	Cross-sectional	Assess the intake and status of selected vitamins and minerals among vegetarian and vegan adults living in Switzerland	In Lausanne/ Zürich, advertisements in schools, restaurants, shops	53 vegans, 53 ovo-lacto-vegetarians 100 omnivores	18-50	Vegans: unsupplemented, or supplement stop 14 days before test	recorded	At least one year	Weight / height Three-day weighed food record Lifestyle factors, physical activity (IPAQ) Alcohol and tobacco  Spot urine Venous blood	EBISpro	Calculated average nutrient intake, Mineral and vitamin status (plasma) A limitation of this study is that originally it was planned to recruit only participants NOT taking vitamin/mineral supplements, it was however difficult to recruit enough vegans not taking supplements, therefore an exception was made for this group, VN subjects had to interrupt supplementation 14 days prior to the start of the study. In the publication the results for supplemented/unsupplemented vegans are not presented separately
Clarys et al. <sup>44</sup>	Belgium	Cross-sectional online survey, with adults	Compare the quality and contributing components of vegan, vegetarian, semi-vegetarian, pesco-vegetarian and omnivorous diets	Through the "Ethical Vegetarian Alternative" organisation, and Ghent University, no exclusion criteria	Vegan, n=104 Vegetarian n=573 Semi-vegetarians n=498 Pesco-vegetarians n=145 Omnivores n=155	> 20 years	After analysis of FFQ and questionnaire (some reclassification necessary, due to differences between self-declared diet and FFQ)	Not taken into account	Not recorded?	52-item FFQ based on the Belgian Food Consumption Survey FFQ + typical products for vegans/vegetarians) Diet questionnaire	SPSS, Belgian FCDB	Scoring according to healthy eating Index 2010, Mediterranean Diet Score (MDS) Limitation: 52-item FFQ – does it cover food items for all diet groups? Not representative (due to higher education level)
Bradbury et al. <sup>43</sup>	UK	Cross-sectional	Compare intakes of major protein sources	UK Biobank, Prospective cohort study recruiting through NHS, only participants of white ethnicity (rationale: the selection of food items for the 24h recall)	90'742 regular meat-eaters 97'124 low meat-eaters 2'259 poultry-eaters 5'701 fish eaters 3'870 vegetarians 248 vegans (102 m, 146 f)	40-69	Based on responses to dietary questions	Not mentioned (not assessed?)	Not reported	24-h, web-based, with 206 food items, 32 drinks		No SDs given, Protein sources were: meat & fish, dairy and plant milk, cheese, yoghurt and eggs. Legumes, nuts and vegetarian alternatives, these products together accounted for 14.8% of the total caloric intake Cereals were not included in the list of "major protein sources" A rough estimate of protein intake due to cereals: approx. 180 g / day bread/pasta other cereal-based products, at approx. 10% protein = 18 g protein, to be added to the protein intake

Derie-maeker et al. <sup>146</sup>	NL / B	Matched/cross-sectional	Compare nutritional and physical characteristics in matched samples of institutionalized vegetarian and non-vegetarian elderly	Recruited directly in senior citizens' homes (in the NL), one vegetarian, one regular (Dutch-speaking part of Belgium)	VG: 22f, 7m Non-VG: 23 f, 7 m	Mean ages F: 84.1 +/- 5.1 M: 80.5 +/- 7.5	Not specified	Not mentioned (not assessed?)	Not reported	FFQ (semi-quantitative, with 104 food items) Blood profile Anthropometrics Handgrip strength	Not directly reported, but reference is given to a prior work	Calculated intakes and blood samples showed similar results. The effect of institutionalization (with prepared foods, with possible supervision of a dietician, and possible mandatory supplementation) is not discussed
Allès et al. <sup>46</sup>	France	Cross-sectional	Describe sociodemographic and nutritional characteristics of self-reported adult vegetarians and vegans compared to meat-eaters	NutriNet-Santé study cohort Web-based, recruiting among Internet-using adults	Vegans n=789 Vegetarians n=2370 Meat-eaters n=90'664	Different age groups (18-30, 30-50, 50-65, 65+)	Pesco-vegetarians classified as vegetarians According to the 3 groups, with direct comparisons: vegetarian vs meat-eaters, and vegans vs. meat-eaters, and in part for vegans vs vegetarians	Not taken into account		Base-line questions of specific diets 3 * 24-h records, web-based, meal-based approach, with 250 food items in a validated picture booklet (and 1000 generic foods)	Published specific FCDB	Results adjusted for sex, age, total energy intakes and a specific "modified programme national Nutrition Santé Guideline Score (mPNNS-GS); Results given as mean intakes food groups in mean g and SEM The adjustment makes comparisons with other studies more difficult
Sobiecki et al. <sup>42</sup>	UK	Cross-sectional	Estimate and compare mean daily nutrient intakes between 4 diet groups, and compare with recommended dietary targets (EARs)	EPIC-Oxford cohort, recruiting based on the 3 <sup>rd</sup> follow-up questionnaire in 2010	"meat-eaters" n=3'798 "fish-eaters" n=782, "vegetarians" n=1'516, "vegans" n = 269	Meat-eaters 63.3 +/- 11.7 Fish-eaters 58.3 +/- 11.2 Vegetarians 56.1 +/- 11.0 Vegans 54.2 +/- 11.1	Categories "meat-eaters", "fish-eaters", "vegetarians", "vegans" based on response to questions	Yes, and detailed	Average 14.3 years after recruitment (range 10.5-18.6)	Diet & lifestyle questionnaires, diet: 112-item semi-quantitative FFQ, based on validated 130-item FFQ	Partially based on manufacturers data	This is one of the studies with most details on supplementation. Data are not shown but it is stated in the text that 1/3 of the calcium intake in the vegan group was provided by plant-based dairy substitutes (largely by fortified varieties) EAR values, as per UK Dept. Health, 1991, do not correspond to DACH values
Appleby et al. <sup>62</sup>	UK	Cross-sectional	Examine the association of fracture risk with diet groups	EPIC-Oxford cohort, recruiting based on the 2 <sup>nd</sup> follow-up questionnaire in 2010	"meat-eaters" n=19'249 "fish-eaters" n=4'901, "vegetarians" n=9'420, "vegans" 1'126		Diet categories + adjustment by age group, other non dietary lifestyle factors (e.g. smoking, PAL, HRT in women)		Average 5 years after recruitment	calcium		Cut-off of 525 mg / day corresponded to the UK estimated average requirement (EAR)

## Appendix III

Comparative relative risk of CVD and cancer morbidity and mortality by sex and type of diet in comparison to non-vegetarian diets in the prospective cohort studies.

NCDs	SDA-Studies [DRR, RR, HR or SIR (95% CI)]		non-SDA-Studies [DRR, RR, HR or SIR (95% CI)]		All studies [DRR, RR, HR or SIR (95% CI)]	
	vegan diets	vegetarian diets	vegan diets	vegetarian diets	vegan diets	vegetarian diets
<b>Incidence</b>						
<b>CVD</b>	NR	NR	NR	NR	NR	NR
	NR	NR	NR	NR	NR	NR
<b>IHD</b>	NR	<b>0.91</b> (0.85–0.98) <sup>a</sup>	NR	<b>0.68</b> (0.58 to 0.81) <sup>b</sup>	NR	NR
"	NR	<b>0.87</b> (0.80–0.96) <sup>a</sup>	NR	NR	NR	NR
<b>CerVD</b>	NR	<b>0.96</b> (0.88–1.04) <sup>a</sup>	NR	NR	NR	NR
"	NR	<b>0.93</b> (0.84–1.03) <sup>a</sup>	NR	NR	NR	NR
<b>Cancers (all)</b>	<b>0.86</b> (0.73 - 1.00) <sup>c</sup>	<b>0.92</b> (0.85 - 1.00) <sup>c</sup>	<b>0.82</b> (0.68, 1.00) <sup>d</sup>	<b>0.90</b> (0.84, 0.97) <sup>d</sup>	<b>0.85</b> (0.75 - 0.95) <sup>e</sup>	<b>0.92</b> (0.87 - 0.98) <sup>e</sup>
- in males (all)	<b>0.81</b> (0.64 - 1.02) <sup>c</sup>	<b>0.92</b> (0.81 - 1.03) <sup>c</sup>	NR	NR	NR	NR
- males cancers	<b>0.81</b> (0.57 - 1.17) <sup>c</sup>	<b>0.94</b> (0.42 - 2.07) <sup>c</sup>	NR	NR	NR	NR
- females	<b>0.91</b> (0.75 - 1.11) <sup>c</sup>	<b>0.93</b> (0.84 - 1.03) <sup>c</sup>	NR	NR	NR	NR
- females cancers	<b>0.71</b> (0.50 - 1.01) <sup>c</sup>	<b>0.97</b> (0.84 - 1.13) <sup>c</sup>	NR	NR	NR	NR
- Breast	<b>0.84</b> (0.62 - 1.13) <sup>d</sup>	<b>1.00</b> (0.87 - 1.16) <sup>d</sup>	<b>0.91</b> (0.61 - 1.34) <sup>e</sup>	<b>0.91</b> (0.77 - 1.08) <sup>f</sup>	NR	NR
- Colorectum	<b>0.86</b> (0.59 - 1.24) <sup>g</sup>	<b>0.79</b> (0.64–0.97) <sup>g</sup>	<b>1.31</b> (0.82 - 2.11) <sup>e</sup>	<b>1.04</b> (0.84, 1.28) <sup>e</sup>	NR	NR
- Prostate	<b>0.66</b> (0.50 - 0.87) <sup>h</sup>	<b>0.96</b> (0.83, 1.12) <sup>h</sup>	<b>0.61</b> (0.31 - 1.20) <sup>e</sup>	<b>0.83</b> (0.64 - 1.06) <sup>e</sup>	NR	NR
<b>Mortality</b>						
<b>CVD</b>	<b>0.91</b> (0.71 – 1.16) <sup>j</sup>	<b>0.87</b> (0.75 – 1.01) <sup>j</sup>	<b>1.21</b> (0.88 – 1.66) <sup>k</sup>	<b>1.12</b> (0.96 – 1.30) <sup>k</sup>	NR	<b>0.93</b> (0.86 – 1.00) <sup>i</sup>
- in males	<b>0.58</b> (0.71 – 0.89) <sup>j</sup>	<b>0.71</b> (0.57 – 0.90) <sup>j</sup>			NR	<b>0.91</b> (0.71 – 1.16) <sup>j</sup>
- in females	<b>1.18</b> (0.88 – 1.60) <sup>j</sup>	<b>0.99</b> (0.83 – 1.18) <sup>j</sup>			NR	<b>0.87</b> (0.75 – 0.90) <sup>j</sup>
<b>IHD</b>	NR	<b>0.70</b> (0.60 – 0.82) <sup>i</sup>	NR	<b>0.79</b> (0.71 – 0.88) <sup>i</sup>	NR	<b>0.75</b> (0.68 – 0.82) <sup>i</sup>
"	<b>0.90</b> (0.60 – 1.33) <sup>j</sup>	<b>0.81</b> (0.64 – 1.02) <sup>j</sup>	<b>0.90</b> (0.53 – 1.5) <sup>k</sup>	<b>1.04</b> (0.83 – 1.30) <sup>k</sup>	NR	
"	NR	<b>0.60</b> (0.43 – 0.83) <sup>j</sup>	NR	<b>0.84</b> (0.74 – 0.84) <sup>j</sup>	NR	NR
<b>CerVD</b>	NR		<b>1.61</b> (0.97 – 2.69) <sup>k</sup>	<b>1.15</b> (0.88 – 1.50) <sup>k</sup>	NR	<b>0.93</b> (0.78 – 1.10) <sup>i</sup>
"	NR	<b>0.71</b> (0.41 – 1.20) <sup>j</sup>	NR	<b>1.05</b> (0.41 – 1.20) <sup>j</sup>	NR	NR
<b>Cancer (all)</b>	<b>0.92</b> (0.68 – 1.24) <sup>j</sup>	<b>0.92</b> (0.78 – 1.28) <sup>j</sup>	<b>1.10</b> (0.85 – 1.42) <sup>k</sup>	<b>0.89</b> (0.78, 1.01) <sup>k</sup>	NR	<b>0.98</b> (0.86 – 1.11) <sup>i</sup>
- in males	<b>0.81</b> (0.48 – 1.36) <sup>j</sup>	<b>1.02</b> (0.78– 1.32) <sup>j</sup>	NR	NR	NR	NR
- in females	<b>0.99</b> (0.69– 1.44) <sup>j</sup>	<b>0.87</b> (0.71 – 1.07) <sup>j</sup>	NR	NR	NR	NR
- Breast	NR	<b>0.57</b> (0.34 – 0.95) <sup>j</sup>	NR	<b>1.40</b> (0.98 – 2.01) <sup>i</sup>	NR	<b>0.94</b> (0.56 – 1.58) <sup>i</sup>
"	NR	NR	NR	<b>1.12</b> (0.77 – 1.63) <sup>k</sup>	NR	NR
- Colorectum	NR	NR	NR	<b>1.11</b> (0.79 – 1.58) <sup>k</sup>	NR	<b>0.90</b> (0.76 – 1.05) <sup>i</sup>
- Prostate	NR	NR	NR	NR	NR	<b>0.90</b> (0.63 – 1.29) <sup>i</sup>
- Lung	NR	NR	NR	<b>1.12</b> (0.77 – 1.63) <sup>k</sup>	NR	<b>0.86</b> (0.62 – 1.19) <sup>i</sup>
<b>Total mortality</b>	NR	<b>0.84</b> (0.78 – 0.90) <sup>j</sup>	NR	<b>1.04</b> (0.84 – 1.10) <sup>i</sup>	<b>0.88</b> (0.75 – 1.02) <sup>j</sup>	<b>0.94</b> (0.86 – 1.04) <sup>i</sup>
"	NR	<b>0.68</b> (0.45 - 1.02) <sup>j</sup>	NR	<b>1.04</b> (0.98 - 1.10) <sup>j</sup>	NR	NR
"	<b>0.85</b> (0.73 – 1.01) <sup>j</sup>	<b>0.88</b> (0.80 – 0.97) <sup>j</sup>	<b>1.11</b> (0.94 – 1.30) <sup>k</sup>	<b>0.98</b> (0.90 – 1.06) <sup>k</sup>	NR	NR
- in males	<b>0.72</b> (0.56 – 0.92) <sup>j</sup>	<b>0.82</b> (0.72 – 0.94) <sup>j</sup>			NR	NR
- in females	<b>0.97</b> (0.70 – 1.22) <sup>j</sup>	<b>0.93</b> (0.82 – 1.05) <sup>j</sup>			NR	NR

Statistically significant if DRR, RR, HR or SIR does not fall in the 95% IC. NR = not reported

DRR = death rate ratios ; RR = risk ratio; HRs = Cox proportional hazards regression; SIRs = Standardized incidence ratios); 95% CI = Confidence interval

Data reported from: <sup>a</sup>Christiansen et al.<sup>192</sup>, 2015 ; <sup>b</sup>Crowe et al.<sup>191</sup>, 2013; <sup>c</sup>Tantamango-Bartley Y et al.<sup>202</sup>, 2013 ; <sup>d</sup>Penniecook-Sawyers JA et al.<sup>208</sup>, 2016; <sup>e</sup>Key TJ et al.<sup>197</sup>, 2014; <sup>f</sup>Key TJ et al.<sup>201</sup>, 2009; <sup>g</sup>Orlich et al.<sup>203</sup>, 2015; <sup>h</sup>Tantamango-Bartley Y et al.<sup>209</sup>, 2016; <sup>i</sup>Dinu et al.<sup>195</sup>, 2017; <sup>j</sup>Orlich et al.<sup>196</sup>, 2013; <sup>k</sup>Appleby et al.<sup>41</sup>, 2016; <sup>l</sup>Kwok et al.<sup>194</sup>, 2014.

# Appendix IV

## Recent studies on the associations between eating disorders and vegetarian / vegan diets

Authors	Study objectives	Methods	Results
Michalak et al. <sup>251</sup> 2012	Matching between dietary groups, prevalence of eating disorders	Munich Composite International Diagnostic Interview (M-CIDI), Questionnaire with questions assessing possible vegetarian diets and their duration (1 month / 12 month / lifetime)	<p>Completely vegetarian group (n=54)</p> <ul style="list-style-type: none"> <li>1-month: 3.7% prevalence</li> <li>12-month: 3.7% prevalence</li> <li>Lifetime : 5.6</li> </ul> <p>Predominantly vegetarian (n=190)</p> <ul style="list-style-type: none"> <li>1-month: 1.1% prevalence</li> <li>12-month: 1.6% prevalence</li> <li>Lifetime : 3.2% prevalence</li> </ul> <p>Non-vegetarian (n=3872)</p> <ul style="list-style-type: none"> <li>1-month: 0.1% prevalence</li> <li>12-month: 0.3% prevalence</li> <li>Lifetime : 0.6% prevalence</li> </ul> <p>Non-vegetarian, matched (n=242)</p> <ul style="list-style-type: none"> <li>1-month: 0.0% prevalence</li> <li>12-month: 0.8% prevalence</li> <li>Lifetime : 1.2% prevalence</li> </ul>
Timko et al. (Timko, 2012 #4412012	Assessing level of vegetarianism, and eating pathologies	Self-assessment, controlled with a specific FFQ, including typical vegetarian items eating behaviour was assessed with 15 independent variables, e.g. Dutch eating behaviour questionnaire, self-esteem scale, eating attitudes test, food acceptance and action questionnaire etc.	<p>Vegans (n=35) Vegetarians (n=111) Semi-vegetarians (n=75) Non-vegetarians (n=265)</p> <p>This study concluded that the sample was "overall rather healthy, the semi-vegetarian group was relatively the most disordered in terms of their food-related behaviours and attitudes".</p>
Zuromski et al. <sup>255</sup> 2015	Investigating the prevalence of vegetarianism within 3 female samples with varying severity of eating disorders	Participants were classified in 3 groups: non-clinical / subclinical / clinical eating disorders (with a battery of questionnaires, including an eating disorder examination-questionnaire. A specific vegetarianism questionnaire was used to verify self-identification as vegetarian or vegan.	<p>Non-clinical group (n=73)</p> <ul style="list-style-type: none"> <li>Vegan: 0.00%</li> <li>Ovo-lacto-vegetarian: 2.7%</li> <li>Pesco-vegetarian: 0.00%</li> <li>Non-vegetarian: 97.3</li> </ul> <p>Subclinical (n=136)</p> <ul style="list-style-type: none"> <li>Vegan: 0.7%</li> <li>Ovo-lacto-vegetarian: 2.90</li> <li>Pesco-vegetarian: 0.70%</li> <li>Non-vegetarian: 95.60%</li> </ul> <p>Clinical (n=69)</p> <ul style="list-style-type: none"> <li>Vegan: 8.70%</li> <li>Ovo-lacto-vegetarian: 18.80%</li> <li>Pesco-vegetarian: 1.40%</li> <li>Non-vegetarian: 71.00%</li> </ul>
Bardone-Cone et al. <sup>254</sup> 2012	Understand rates of vegetarianism in analyses related to eating disorders	Self-assessment on dietary type and duration Eating disorder recovery status Eating disorder examination questionnaire	<p>No eating disorder history (n=67)</p> <ul style="list-style-type: none"> <li>Ever vegetarian: 11.9</li> <li>Current vegetarian: 6.0</li> <li>Weight-related reason: 0%</li> </ul> <p>Eating disorder history (n=93)</p> <ul style="list-style-type: none"> <li>Ever vegetarian: 51.6%</li> <li>Current vegetarian: 23.7%</li> <li>Weight-related reason: 42.2%</li> </ul> <hr/> <p>Fully recovered (n=19)</p> <ul style="list-style-type: none"> <li>Ever vegetarian: 57.9%</li> <li>Current vegetarian: 5.3%</li> <li>Weight-related reason: 22.2%</li> </ul> <p>Partially recovered (n=15)</p> <ul style="list-style-type: none"> <li>Ever vegetarian: 33.3%</li> <li>Current vegetarian: 13.3%</li> <li>Weight-related reason: 50.0%</li> </ul> <p>Active eating disorder (n=52)</p> <ul style="list-style-type: none"> <li>Ever vegetarian: 53.8%</li> <li>Current vegetarian: 32.7%</li> <li>Weight-related reason: 46.4%</li> </ul>
Forestell et al. 2012 <sup>256</sup>	Compare eating and dieting patterns and personality characteristics (college females, n=240)	General eating habits (at base-line and one year after), self-chosen category (vegan, lactovegetarian, ovo-vegetarian, pesco-vegetarian, semi-vegetarian, flexitarian, omnivore, + various eating habit questionnaires, e.g. Eating Attitude Test (EAT), Food Neophobia and Variety Seeking	Vegans (n=14), lactovegetarians (n=6), and ovo-lacto-vegetarians (n=35) were combined: "vegetarians... were not more restrained than omnivores. Rather semi-vegetarians (...) were significantly more restrained than omnivores."
Heiss et al. <sup>252</sup> 2017	Compare vegan to demographically comparable omnivores	Self-reported vegans + various eating disorder questionnaires, e.g. Eating Disorder Examination Questionnaire (EDE-Q)	Vegans (n=357) and omnivores (n=220) "vegans scored significantly lower on the EFE-Q subscales "restraint", "eating concern", "shape concern", the results "confirm that they (vegans) do not experience greater eating-related pathologies than their omnivorous counterparts"